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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Apr 08	"Ask CAS" for self-help around the clock
NEWS 3	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 4	Apr 09	ZDB will be removed from STN
NEWS 5	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 6	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 7	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 8	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 9	Jun 03	New e-mail delivery for search results now available
NEWS 10	Jun 10	MEDLINE Reload
NEWS 11	Jun 10	PCTFULL has been reloaded
NEWS 12	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS 13	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
NEWS 14	Jul 29	Enhanced polymer searching in REGISTRY
NEWS 15	Jul 30	NETFIRST to be removed from STN
NEWS 16	Aug 08	CANCERLIT reload
NEWS 17	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 18	Aug 08	NTIS has been reloaded and enhanced
NEWS 19	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 20	Aug 19	IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21	Aug 19	The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 23	Sep 03	JAPIO has been reloaded and enhanced
NEWS 24	Sep 16	Experimental properties added to the REGISTRY file
NEWS 25	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 26	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 27	Oct 21	EVENTLINE has been reloaded
NEWS 28	Oct 24	BEILSTEIN adds new search fields
NEWS 29	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 30	Oct 25	MEDLINE SDI run of October 8, 2002
NEWS 31	Nov 18	DKILIT has been renamed APOLLIT
NEWS 32	Nov 25	More calculated properties added to REGISTRY
NEWS 33	Dec 02	TIBKAT will be removed from STN
NEWS 34	Dec 04	CSA files on STN
NEWS 35	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 36	Dec 17	TOXCENTER enhanced with additional content
NEWS 37	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 38	Dec 30	ISMEC no longer available
NEWS 39	Jan 21	NUTRACEUT offering one free connect hour in February 2003
NEWS 40	Jan 21	PHARMAML offering one free connect hour in February 2003
NEWS 41	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 42	Feb 13	CANCERLIT is no longer being updated
NEWS 43	Feb 24	METADEX enhancements
NEWS 44	Feb 24	PCTGEN now available on STN
NEWS 45	Feb 24	TEMA now available on STN
NEWS 46	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 47	Feb 26	PCTFULL now contains images

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 NEWS 48  Mar 04  SDI PACKAGE for monthly delivery of multifile SDI results
 NEWS 49  Mar 19  APOLLIT offering free connect time in April 2003
 NEWS 50  Mar 20  EVENTLINE will be removed from STN
 NEWS 51  Mar 24  PATDPAFULL now available on STN
 NEWS 52  Mar 24  Additional information for trade-named substances without
                  structures available in REGISTRY
 NEWS 53  Mar 24  Indexing from 1957 to 1966 added to records in CA/CAPLUS

 NEWS EXPRESS  January 6 CURRENT WINDOWS VERSION IS V6.01a,
               CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
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 NEWS WWW      CAS World Wide Web Site (general information)

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FILE COVERS 1907 - 2 Apr 2003  VOL 138 ISS 14
FILE LAST UPDATED: 1 Apr 2003  (20030401/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


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E1            1     CA1078722/PN
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E7            2      CA1078735/PN
E8            1      CA1078736/PN
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E10           1      CA1078738/PN
E11           1      CA1078739/PN
E12           1      CA1078747/PN

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L1            1 CA1078731/PN

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L1 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1978:559612 HCAPLUS
DOCUMENT NUMBER: 89:159612
TITLE: Kit for the preparation of an injectable technetium-99m-containing solution as well as a method for the preparation of an improved injectable solution for bone imaging
PATENT ASSIGNEE(S): Frosst, Charles E., and Co., Can.
SOURCE: Neth. Appl., 9 pp.
CODEN: NAXXAN
DOCUMENT TYPE: Patent
LANGUAGE: Dutch
INT. PATENT CLASSIF.: A61K043-00
CLASSIFICATION: 8-1 (Radiation Biochemistry)
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
NL 7713161	A	19780620	NL 1977-13161	19771129
CA 1078731	A1	19800603	CA 1976-268001	19761216 <--
FR 2374014	A1	19780713	FR 1977-37497	19771213
FR 2374014	B1	19800404		
BE 861923	A1	19780616	BE 1977-183512	19771216
JP 53077016	A2	19780708	JP 1977-150748	19771216

PRIORITY APPLN. INFO.: CA 1976-268001 19761216
ABSTRACT:
A lyophilized soln. of triethylenetetraminehexa(methylenephosphonic acid) (I) and SnCl2 in a sterile ampul is reconstituted with sterile saline contg. Na99mTcO4 to form a 99mTc complex which may be injected i.v. for bone scintigraphy. Thus, 100 mg I and 2.5 mg SnCl2.2H2O are dissolved in 20 mL sterile distd. water, the pH adjusted to 4, the soln. divided into 2 mL portions, placed in 10 mL ampuls, and lyophilized under aseptic conditions. At the time of use, 2-8 mL sterile saline contg. .apprx.40 mCi Na99mTcO4 is added to each ampul and the soln. made up to 10 mL with saline. I is prepd. by refluxing triethylenetetramine-4HCl with PCl3 in aq. soln. with dropwise addn. of CH2O. I was pptd. with Pb(NO3)2, and Pb was then removed with H2S as PbS.

SUPPL. TERM: technetium 99m complex bone scintigraphy
INDEX TERM: Scintigraphy
(of bone, metastable technetium-99 complex for)
INDEX TERM: Bone
(scintigraphy of, metastable technetium-99 complex for)
INDEX TERM: 7440-31-5D, technetium-99-triethylenetetraminehexa(methylene phosphonic acid) complex 14133-76-7D, tin-triethylenetetraminehexa(methylenephosphonic acid) complex 36475-52-2D, technetium-99-tin complex
ROLE: BIOL (Biological study)
(metastable, for bone scintigraphy)
INDEX TERM: 4961-40-4
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with formaldehyde and phosphorus trichloride)

L1 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)
INDEX TERM: 7719-12-2
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with formaldehyde and triethylenetetramine)
INDEX TERM: 50-00-0, reactions
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with phosphorus trichloride and triethylenetetramine)

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E3            1 --> EP164843/PN
E4            1      EP164844/PN
E5            1      EP164848/PN
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E7            1      EP164852/PN
E8            1      EP164853/PN
E9            1      EP164855/PN
E10           1      EP164856/PN
E11           2      EP164860/PN
E12           1      EP164864/PN

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L2            1 EP164843/PN

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L2 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1986:221459 HCAPLUS
DOCUMENT NUMBER: 104:221459
TITLE: Organic amine phosphonic acid complexes for the treatment of calcific tumors
INVENTOR(S): Simon, Jaime; Volkert, Wynn A.; Wilson, David A.; Troutner, David E.; Goeckeler, William F.
PATENT ASSIGNEE(S): Dow Chemical Co., USA
SOURCE: Eur. Pat. Appl., 38 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K043-00
CLASSIFICATION: 8-9 (Radiation Biochemistry)
Section cross-reference(s): 1, 29
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 164843	A2	19851218	EP 1985-302634	19850415 <--
EP 164843	A3	19870923		
EP 164843	B1	19910619		
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
AU 8541229	A1	19851212	AU 1985-41229	19850415
AU 563671	B2	19870716		
ZA 8502799	A	19861230	ZA 1985-2799	19850415
IL 74902	A1	19901223	IL 1985-74902	19850415
JP 61022029	A2	19860130	JP 1985-79430	19850416
JP 06055681	B4	19940727		
CA 1243603	A1	19881025	CA 1985-479260	19850416
JP 62132892	A2	19870616	JP 1985-271679	19851204
JP 04048799	B4	19920807		

PRIORITY APPLN. INFO.: US 1984-616985 A 19840604
ABSTRACT:
Phosphonic acid derivs. of org. amines having N and P linked by an alkylene group, complexed with particle-emitting radionuclides (e.g., 153Sm, 175Yb, 177Lu,, 159Gd) are useful in the treatment of calcific tumors (bone metastases). Ethylenediaminetetramethylenephosphonic acid (EDTMP), diethylenetriaminepentamethylenephosphonic acid (DTPMP), hydroxyethylethylenediaminetrimethylenephosphonic acid (HEEDTMP), and tris(2-aminoethyl)aminehexamethylenephosphonic acid (TTHMP) were prepd. by the reaction of corresponding amines with H3PO3 followed by reaction with HCHO. Nitrilotrimethylenephosphonic acid (NTMP) was prepd. by the reaction of NH4Cl with H3PO3 followed by reaction with HCHO. EDTMP, DTPMP, HEEDTMP, and TTHMP were complexed with 153Sm; EDTMP, DTPMP, HEEDTMP, and NTMP were complexed with 175Yb; and EDTMP and HEEDTMP were complexed with 177Lu and 159Gd. Rats injected i.v. with EDTMP, DTPMP, HEEDTMP, or TTHMP complexed with 153Sm (50-100
.mu.L) were sacrificed after 2 h. Organs were removed and counted for biolocalization. A significant amt. (28-58%) of radioactivity was concd. in the skeletal system with a very little soft tissue uptake. Similar results were also obsd. with other complexes in rats and rabbits. Two non-N-contg. phosphonic acid derivs., 1-hydroxyethylidene-1,1-diphosphonic acid (HEDP) and methylenediphosphonate (MDP) were complexed with 153Sm. The Sm-MDP exhibited undesirable high liver uptake and Sm-HEDP showed a low skeletal uptake with poor blood clearance.

L2 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)

SUPPL. TERM: aminophosphonate radionuclide complex prepn; calcific tumor treatment aminophosphonate complex; samarium aminophosphonate complex tumor treatment; ytterbium aminophosphonate complex tumor treatment; lutetium aminophosphonate complex tumor treatment; gadolinium aminophosphonate complex tumor treatment; bone metastasis treatment aminophosphonate radionuclide
INDEX TERM: Neoplasm inhibitors
(aminophosphonate radionuclide complexes)
INDEX TERM: Radiotherapy
(of bone metastasis, with aminophosphonate radionuclide complexes)
INDEX TERM: Bone, neoplasm
(metastasis, aminophosphonate radionuclide complexes for treatment of)
INDEX TERM: 13967-65-2D, aminophosphonate complexes 14041-42-0D, aminophosphonate complexes 14041-44-2D, aminophosphonate complexes 14265-75-9D, aminophosphonate complexes 15766-00-4D, aminophosphonate complexes
ROLE: BIOL (Biological study)
(bone metastasis treatment with)
INDEX TERM: 1429-50-1DP, radionuclide complexes 6419-19-8DP, radionuclide complexes 15827-60-8DP, radionuclide complexes 32685-03-3DP, radionuclide complexes 102502-26-1DP, radionuclide complexes
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for bone metastasis treatment)

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E2            1     EP210041/PN
E3            1 --> EP210043/PN
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L3            1 EP210043/PN

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L3 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1988:128096 HCAPLUS
DOCUMENT NUMBER: 108:128096
TITLE: Amino phosphonate-cation complexes as contrast agents for NMR scanning of calcified tissues
INVENTOR(S): Sadler, Peter John; Harding, Charles Thomas; Kelly, James Duncan; McEwen, Andrew Bruce
PATENT ASSIGNEE(S): Amersham International PLC, UK
SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 210043	A2	19870128	EP 1986-305462	19860716 <--
EP 210043	A3	19880817		
EP 210043	B1	19920108		
R: DE, FR, GB				
US 4880007	A	19891114	US 1986-884622	19860711
JP 62042934	A2	19870224	JP 1986-169666	19860718
JP 2516599	B2	19960724		
PRIORITY APPLN. INFO.:			GB 1985-18300	19850719

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L3 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1988:128096 HCAPLUS
DOCUMENT NUMBER: 108:128096
TITLE: Amino phosphonate-cation complexes as contrast agents for NMR scanning of calcified tissues
INVENTOR(S): Sadler, Peter John; Harding, Charles Thomas; Kelly, James Duncan; McEwen, Andrew Bruce
PATENT ASSIGNEE(S): Amersham International PLC, UK
SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K049-00
SECONDARY: C07F009-38
CLASSIFICATION: 9-1 (Biochemical Methods)
Section cross-reference(s): 14
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 210043	A2	19870128	EP 1986-305462	19860716 <--
EP 210043	A3	19880817		
EP 210043	B1	19920108		
R: DE, FR, GB				
US 4880007	A	19891114	US 1986-884622	19860711
JP 62042934	A2	19870224	JP 1986-169666	19860718
JP 2516599	B2	19960724		

PRIORITY APPLN. INFO.: GB 1985-18300 19850719
ABSTRACT:
Contrast agents for scanning of calcified tissue by NMR are prepd. which comprise complexes between (1) an amino di- or poly-phosphonate in which the phosphonate group comprise different C atoms, and (2) a paramagnetic metal ion.
A complex of Gd with diethylenetriamine tetramethylphosphonate (EDTMP) was prepd. by mixing 0.043 g Gd(NO3)3.5H2O with 0.046 g EDTMP in 5 mL acetate buffer pH 5.6. One mL of 1M NaOH was added, followed by 4 mL of acetate buffer
to give a 1 mM soln. of the complex.

SUPPL. TERM: NMR contrast agent calcified tissue; gadolinium amine phosphonate NMR contrast agent
INDEX TERM: Tomography
(NMR, of calcified tissues, amino phosphonate-cation complexes as contrast agents for)
INDEX TERM: Animal tissue
(calcified, scanning of, by NMR, amino phosphonate-cation
complexes as contrast agents for)
INDEX TERM: Cations
(paramagnetic, complexes, with amino di- or polyphosphonates, as contrast agents for NMR scanning of calcified tissues)
INDEX TERM: 1429-50-1D, cation complexes 2439-99-8D, cation complexes 5995-42-6D, cation complexes 15827-60-8D, methal complexes

L3 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)
36475-52-2D, cation complexes 41318-17-6D, cation complexes 41318-26-7D, cation complexes 54622-43-4D, cation complexes 55628-97-2D, cation complexes 55628-98-3D, cation complexes 75125-54-1D, cation complexes 82460-73-9D, cation complexes 82460-74-0D, cation complexes 107611-72-3 107611-73-4 107611-74-5 107611-75-6 107611-76-7 107611-77-8 107611-78-9 107634-93-5D, cation complexes 107635-99-4 107636-00-0 107673-78-9
ROLE: ANST (Analytical study)
(as contrast agent for NMR scanning of calcified tissues)
INDEX TERM: 1306-06-5D, adduct with amino di- or poly-phosphonate-metal complexes
ROLE: ANST (Analytical study)
(as contrast agents for NMR imaging of gastrointestinal tract)
INDEX TERM: 13598-36-2D, amino poly-, paramagnetic cation complexes
ROLE: ANST (Analytical study)
(as contrast agents for NMR scanning of calcified tissue)
INDEX TERM: 7439-89-6D, di- or poly-phosphonate complexes 7439-96-5D, Manganese, amino di- or poly-phosphonate complexes 7440-47-3D, Chromium, amino di- or poly-phosphonate complexes 7440-54-2D, di- or poly-phosphonate complexes
ROLE: ANST (Analytical study)
(as contrast agents for NMR scanning of calcified tissues)
INDEX TERM: 107673-79-0
ROLE: ANST (Analytical study)
(as paramagnetic agent for NMR scanning of calcified tissues)
INDEX TERM: 107611-71-2P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as contrast agents for NMR scanning of calcified tissues)

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E10           1     EP232770/PN
E11           1     EP232772/PN
E12           1     EP232776/PN

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L4            1 EP232751/PN

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L4 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1988:56130 HCAPLUS
DOCUMENT NUMBER: 108:56130
TITLE: Preparation of 1-substituted-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane and analogs as medical imaging agents
INVENTOR(S): Tweedle, Michael F.; Gaughan, Glen T.; Hagan, James J.
PATENT ASSIGNEE(S): Squibb, E. R., and Sons, Inc. , USA
SOURCE: Eur. Pat. Appl., 13 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07D273-00
SECONDARY: C07D257-02; A61K049-00; A61K049-04
CLASSIFICATION: 28-23 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 8, 29
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 232751	A1	19870819	EP 1987-100635	19870119 <--
EP 232751	B1	19910911		
R: BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 62190175	A2	19870820	JP 1987-15037	19870122
JP 2537502	B2	19960925		

PRIORITY APPLN. INFO.: US 1986-821725 19860123
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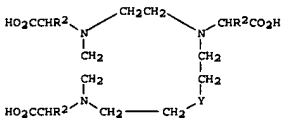

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ABSTRACT:
The title compds. (I; Y = O, NR1; R1 = H, alkyl, aralkyl, aryl; R2 = H, alkyl) were prepd. as metal-chelating ligands for use in diagnostic medicine as contrast agents and relaxation enhancement agents. 1-Oxa-4,7,10-triazacyclododecane and ClCH2CO2H in H2O at pH 9.5 were stirred for 15 h at 45.degree. to give I (R2 = H, Y = O) (II). II was added to aq. Gd(OAc)3, the pH adjusted to 3, and the soln. was heated at 88.degree. for 20 min. to give the Gd(III) deriv. of II.

SUPPL. TERM: carboxymethyloxatriazacyclododecane prepn ligand imaging agent; azacyclododecane triscarboxymethyl prepn imaging agent; cyclododecane aza triscarboxymethyl prepn imaging

L4 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)
(Preparation); RACT (Reactant or reagent)
(prepn. and oxidn. of)
INDEX TERM: 112193-82-5P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and redn. of)
INDEX TERM: 23539-10-8P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and tosylation of)
INDEX TERM: 112188-16-6P 112188-17-7P 112188-18-8P 112188-19-9P
112188-20-2P 112188-21-3P 112188-22-4P 112188-23-5P
112188-24-6P 112188-25-7P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as biomedical imaging agent)
INDEX TERM: 112193-74-5P 112193-75-6P 112193-76-7P 112207-13-3P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as ligand for use in biomedical imaging)

L4 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)
agent
INDEX TERM: Radiography
(contrast agents, paramagnetic metal complexes of tetraazacyclododecane as)
INDEX TERM: Sound and Ultrasound, biological effects
(paramagnetic atom-contg. tetraazacyclododecane complexes
as imaging agents for)
INDEX TERM: Imaging
Tomography
(NMR, paramagnetic ion-contg. tetraazacyclododecane complexes for)
INDEX TERM: 79-11-8, Chloroacetic acid, reactions
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(alkylation by, of triazacyclododecane deriv.)
INDEX TERM: 112193-77-8 112207-14-4
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(alkylation of, by chloroacetic acid)
INDEX TERM: 100-46-9, Benzylamine, reactions
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(amination by, of acrylamide)
INDEX TERM: 79-06-1, Acrylamide, reactions
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(amination of, by benzylamine)
INDEX TERM: 7705-08-0, Ferric chloride, reactions 10025-73-7 10025-74-8, Dysprosium chloride 10361-44-1, Bismuth nitrate 11132-78-8, Manganese chloride 12064-62-9 14119-09-6 14133-76-7 16056-77-2
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(conversion of, to tetraazacyclododecane chelate)
INDEX TERM: 16695-22-0, Diethanolamine tritosylate
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation of, with bis(toluenesulfonyl)triazahep
tane)
INDEX TERM: 111-40-0, Diethylenetriamine
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation of, with di-Me benzyliminodiacetate)
INDEX TERM: 6175-26-4
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation of, with diethylenetriamine)
INDEX TERM: 112193-81-4P 112193-83-6P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and alkylation of)
INDEX TERM: 112193-79-0P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and cyclocondensation of, with diethanolamine tritosylate)
INDEX TERM: 112193-80-3P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and detosylation of)
INDEX TERM: 112193-78-9P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP

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E7            1      EP255481/PN
E8            1      EP255482/PN
E9            1      EP255484/PN
E10           1      EP255485/PN
E11           1      EP255486/PN
E12           1      EP25549/PN

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           441 EES
L5       11401 EE
                (EE OR EES)

=> s e3
L6            1 EP255471/PN

=> d iall
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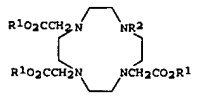
L6 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1988:406552 HCAPLUS
DOCUMENT NUMBER: 109:6552
TITLE: Preparation of 1,4,7,10-tetraazacyclododecane-1,4,7-triacetates and their metal salts and complexes as diagnostic aids for x-ray and tomographic diagnoses
INVENTOR(S): Gries, Heinz; Raduechel, Bernd; Speck, Ulrich; Weinmann, Hanns Joachim
PATENT ASSIGNEE(S): Schering A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 11 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
INT. PATENT CLASSIF.:
MAIN: C07D257-02
SECONDARY: A61K049-00; A61K049-04; A61K043-00; A61K031-555; A61K031-395
ADDITIONAL: A61B005-05
CLASSIFICATION: 28-23 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 8, 63, 78
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3625417	A1	19880211	DE 1986-3625417	19860728
DE 3625417	C2	19981008		
EP 255471	A1	19880203	EP 1987-730085	19870724 <--
EP 255471	B1	19920909		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 80391	E	19920915	AT 1987-730085	19870724
ES 2052599	T3	19940716	ES 1987-730085	19870724
NO 8703132	A	19880129	NO 1987-3132	19870727
NO 174048	B	19931129		
NO 174048	C	19940309		
AU 8776217	A1	19880204	AU 1987-76217	19870727
AU 604249	B2	19901213		
DK 8703933	A	19880129	DK 1987-3933	19870728
DK 171574	B1	19970120		
JP 63041468	A2	19880222	JP 1987-186794	19870728
JP 07053720	B4	19950607		
ZA 8705561	A	19890329	ZA 1987-5561	19870728

PRIORITY APPLN. INFO.: DE 1986-3625417 19860728
EP 1987-730085 19870724
OTHER SOURCE(S): CASREACT 109:6552; MARPAT 109:6552
GRAPHIC IMAGE:

L6 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)



I

ABSTRACT:
The title compds. [I; R1 = H, metal ion equiv.; R2 = H, B, BCOCH2, R3R4NZCH2, (un)satd. C1-10 alkyl, alkanoyl, optionally substituted by OH, alkoxy; B = biomol. residue; R3,R4 = H, C1-16 alkyl, optionally substituted by OH, alkoxy; R3R4N = 5- or 6-membered heterocyclyl; R2,R3 may represent a second tetraazacyclododecane moiety bound via an (un)substituted, difunctional acyl or
hydrocarbon group; Z = CO, C1-10 alkylene, optionally interrupted with O and having OH and alkoxy substituents], their salts, metal complexes, and conjugates with biomols., were prepd. as imaging aids for x-ray, scintigraphic,
and tomog. diagnosis (no data). N, N',N''-Tris(p-tolylsulfonyl)diethylenetriamine di-Na salt and N,N-bis[(p-tolylsulfonyl)oxy]ethyl]benzylamine were heated at 100.degree. in DMF to give 1-benzyl-4,7,10-tris(p-tolylsulfonyl)-1,4,7,10-tetraazacyclododecane. This was detosylated by heating at 50.degree. in HBr/HOAc/PhOH and alkylated with BrCH2CO2Et to give I (R1 = Et, R2 = PhCH2). The latter was debenzylated by hydrogenation over Pd/C, and the resulting triester was sapond. with 3 N NaOH and, without isolation, treated with Gd(OAc)3 and stirred 3 h at 60.degree. to give the Gd(III) complex of I (R1 = R2 =H) (1:1).

SUPPL. TERM: tetraazacyclododecanetriacetate gadolinium complex
diagnostic aid; x ray contrast media
tetraazacyclododecanetriacetate; scintigraphy contrast media
tetraazacyclododecanetriacetate; tomog contrast media
tetraazacyclododecanetriacetate; contrast media
tetraazacyclododecanetriacetate gadolinium complex
INDEX TERM: Radiography
(contrast agents for, tetraazacyclododecanetriacetate gadolinium complexes for)
INDEX TERM: Scintigraphy
(with tetraazacyclododecanetriacetates and their metal complexes)
INDEX TERM: Tomography
(NMR, contrast agents for, tetraazacyclododecanetriacetat
e gadolinium complexes for)
INDEX TERM: 75-04-7, Ethylamine, reactions 40137-22-2, 3-(Methylamino)-1,2-propanediol
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(amidation by, of tetraazacyclododecaneacetate deriv.)
INDEX TERM: 141-43-5, reactions
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(amidation by, of tetraazacyclododecanecarboxylate deriv.)
INDEX TERM: 52601-80-6
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation of, with iminodiethanol tosylate deriv.)
INDEX TERM: 114873-49-3
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation of, with tritosyldiethylenetriamine)
INDEX TERM: 112193-83-6P, 1-Benzyl-1,4,7,10-tetraazacyclododecane
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and alkylation of, by bromo- and chloroacetate)
INDEX TERM: 114873-54-0P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and amidation of)
INDEX TERM: 114873-37-9P 114873-38-0P 114873-39-1P 114873-40-4P
114873-41-5P 114873-42-6P 114873-43-7P 114873-44-8P
114873-45-9P 114873-46-0P 114873-47-1P 114873-48-2P
114903-32-1P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and complexation of, for tomog. and x-ray contrast agents)
INDEX TERM: 114873-51-7P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and debenzylation of)
INDEX TERM: 112193-80-3P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and detosylation of)
INDEX TERM: 114873-52-8P 114873-53-9P 114873-55-1P 114873-56-2P
114873-57-3P 114873-58-4P 114873-59-5P 114873-60-8P
114873-61-9P 114873-62-0P 114873-63-1P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and sapon. and complexation of, with gadolinium)
INDEX TERM: 114873-65-3P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and sapon. of)
INDEX TERM: 114873-64-2P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
INDEX TERM: 112188-16-6P 114757-60-7P 114757-61-8P 114757-62-9P
114757-63-0P 114757-64-1P 114757-65-2P 114758-26-8P
114758-27-9P 114758-28-0P 114758-29-1P 114781-58-7P
114824-40-7P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as tomog. and x-ray contrast agent)
INDEX TERM: 543-20-4, Succinyl chloride 23911-26-4 38870-89-2, Methoxyacetyl chloride
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(N-acylation by, of tetraazacyclododecanetriacetate)
INDEX TERM: 79-11-8, Chloroacetic acid, reactions 96-24-2, 3-Chloro-1,2-propanediol 105-36-2, Ethyl bromoacetate 107-07-3, 2-Chloroethanol, reactions 109-64-8, 1,3-Dibromopropane 7355-58-0
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(N-alkylation by, of tetraazacyclododecane deriv.)

L6 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)

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L7            1 EP258616/PN

=> d iall
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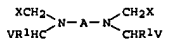
L7 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1988:626271 HCAPLUS
DOCUMENT NUMBER: 109:226271
TITLE: NMR imaging with paramagnetic polyvalent metal salts of poly(acid-alkyleneamino)alkanes as contrast agents
INVENTOR(S): Kraft, Karl F.; Quay, Steve C.; Rocklage, Scott M.; Worah, Dilip
PATENT ASSIGNEE(S): Salutar, Inc., USA
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K049-00
SECONDARY: C07F009-38; C07C101-26; G01N024-02
CLASSIFICATION: 9-5 (Biochemical Methods)
Section cross-reference(s): 78
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
EP 258616	A1	19880309	EP 1987-110801	19870725	<--
EP 258616	B1	19920325			
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE					
US 5039512	A	19910813	US 1987-57709	19870615	
AU 8775735	A1	19880211	AU 1987-75735	19870716	
AU 608759	B2	19910418			
ZA 8705274	A	19880427	ZA 1987-5274	19870717	
CA 1321346	A1	19930817	CA 1987-542735	19870722	
EP 463644	A2	19920102	EP 1991-116072	19870725	
EP 463644	A3	19921119			
EP 463644	B1	19960605			
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE					
AT 74015	E	19920415	AT 1987-110801	19870725	
ES 2030023	T3	19921016	ES 1987-110801	19870725	
AT 138809	E	19960615	AT 1991-116072	19870725	
ES 2087938	T3	19960801	ES 1991-116072	19870725	
SG 78250	A1	20010220	SG 1996-4804	19870725	
DK 8704010	A	19880205	DK 1987-4010	19870731	
DK 167797	B1	19931220			
JP 63119446	A2	19880524	JP 1987-190530	19870731	
NO 8703237	A	19880205	NO 1987-3237	19870803	
NO 173767	B	19931025			
NO 173767	C	19940202			
FI 8703382	A	19880205	FI 1987-3382	19870804	
FI 88677	B	19930315			
FI 88677	C	19930628			
US 5219553	A	19930615	US 1991-743212	19910809	
IL 101210	A1	19961031	IL 1992-101210	19920312	

PRIORITY APPLN. INFO.: US 1986-893136 A 19860804
US 1986-900930 A 19860827
US 1987-57709 A 19870615
EP 1987-110801 A 19870725
OTHER SOURCE(S): MARPAT 109:226271
GRAPHIC IMAGE:

L7 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)



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ABSTRACT:
The title contrast agents are Ca or Mg salts of physiolog. compatible chelates of lanthanide or transition metals, with the general formula I or N(CH2X)3 (II)
[X = CO2Y, PO3HY, CONHOY; Y = H, metal ion equiv. or biocompatible cation (.gtoreq.2 equivs. lanthanide or transition metal, .gtoreq.1 equiv. Ca or Mg); A = CHR2CHR3 etc.; R1 = H, Me; R2,3 = H or (combined) (CH2)3-4; V = X, CH2OH, CONH(CH2)nX; n = 1-12], and are administered in a pharmaceutically acceptable carrier before NMR tomog., to give enhanced images due to shortening of magnetic relaxation times of water mols. The Ca salt of the Mn complex of trans-1,2-diaminocyclohexane-N,N,N',N'-tetramethylenephosphonic acid (DCTP) was
prepd.; at 10-2 M in water it gave spin-lattice (T1) and spin-spin (T2) relaxation times of 16 and 8, resp., vs. 32 and 22 for a similar salt with the analogous tetraacetate ligand; in plasma the values were 15 and 10, resp., vs. 25 and 50.5. The LD50 in mice was 4.9 mmol/kg vs. 0.2 mmol/kg for the tetraacetate complex.

SUPPL. TERM: paramagnetic contrast agent NMR tomog; zeugmatog paramagnetic contrast agent
INDEX TERM: Heart
Intestine
Liver
Pancreas
Spleen
(NMR imaging of, biocompatible paramagnetic contrast agents for)
INDEX TERM: Tomography
(NMR, contrast agents for, biocompatible paramagnetic lanthanide and transition metal complexes)
INDEX TERM: Transition metals, compounds
ROLE: ANST (Analytical study)
(complexes, biocompatible salts, as paramagnetic contrast
agents for NMR tomog.)
INDEX TERM: Rare earth metals, compounds
ROLE: ANST (Analytical study)
(complexes, chelate, biocompatible salts, as paramagnetic
contrast agents for NMR tomog.)
INDEX TERM: Magnetic substances
(para-, biocompatible salts of lanthanide and transition metal chelates, contrast agents for NMR tomog.)
INDEX TERM: Magnetic relaxation
(spin-lattice, enhancement of, paramagnetic agents for, as biocompatible contrast agents for NMR tomog.)
INDEX TERM: Magnetic relaxation
(spin-spin, enhancement of, paramagnetic agents for, as biocompatible contrast agents for NMR tomog.)

L7 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)
INDEX TERM: 117584-71-1P 117584-72-2P 117584-73-3P 117584-74-4P
117584-75-5P 117584-76-6P 117584-83-5P 117584-84-6P
117584-85-7P 117584-86-8P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as biocompatible contrast agent for NMR tomog.)
INDEX TERM: 67-43-6DP, complexes with lanthanide and transition metals, calcium and magnesium salts 93-62-9DP, complexes with lanthanide and transition metals, calcium and magnesium salts 139-13-9DP, Nitrilotriacetic acid, complexes with lanthanide and transition metals, calcium and magnesium salts 150-39-0DP, complexes with lanthanide and transition
metals, calcium and magnesium salts 1429-50-1DP, complexes
with lanthanide and transition metals, calcium and magnesium
salts 7439-89-6DP, ethylenediaminebis(acetic acid)bis(hydroxyphenyl) complexes, calcium or magnesium salts 10328-28-6DP, iron complexes, calcium or magnesium salts 35998-29-9DP, iron complexes, calcium or magnesium salts
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as biocompatible contrast agents for NMR tomog.)
INDEX TERM: 7773-01-5 10138-52-0
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prepn. of contrast agent for NMR tomog.)
INDEX TERM: 13598-36-2
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with diaminocyclohexane, in prepn. of contrast agent for NMR tomog.)
INDEX TERM: 1121-22-8
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with phosphorous acid, in prepn. of contrast agent for NMR tomog.)

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E7            1      EP287471/PN
E8            1      EP287477/PN
E9            1      EP287478/PN
E10           1      EP287479/PN
E11           1      EP287482/PN
E12           1      EP287486/PN

=> s e3
L8            1 EP287465/PN

=> d iall
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L8 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1989:469850 HCAPLUS
DOCUMENT NUMBER: 111:69850
TITLE: Cyclic ligands containing nitrogen, metal complexes formed by these ligands, diagnostic compositions containing them and process for their preparation
INVENTOR(S): Schaeffer, Michel; Doucet, Didier; Bonnemain, Bruno; Meyer, Dominique
PATENT ASSIGNEE(S): Guerbet S. A., Fr.
SOURCE: Eur. Pat. Appl., 26 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
INT. PATENT CLASSIF.:
MAIN: C07D257-02
SECONDARY: C07D259-00; A61K049-00; C07F005-00; C07F015-02; C07F013-00
CLASSIFICATION: 78-7 (Inorganic Chemicals and Reactions)
Section cross-reference(s): 9, 74
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 287465	A1	19881019	EP 1988-400895	19880413 <--
EP 287465	B1	19930127		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FR 2614020	A1	19881021	FR 1987-5288	19870414
FR 2614020	B1	19890728		
NO 8801567	A	19881017	NO 1988-1567	19880412
NO 176839	B	19950227		
NO 176839	C	19950614		
ZA 8802552	A	19881130	ZA 1988-2552	19880412
DD 293113	A5	19910822	DD 1988-314659	19880412
DK 8802027	A	19881015	DK 1988-2027	19880413
DK 170946	B1	19960325		
FI 8801708	A	19881015	FI 1988-1708	19880413
FI 93830	B	19950228		
FI 93830	C	19950612		
HU 47075	A2	19890130	HU 1988-1897	19880413
HU 198501	B	19891030		
JP 01211573	A2	19890824	JP 1988-89189	19880413
IL 86059	A1	19930114	IL 1988-86059	19880413
AT 85052	E	19930215	AT 1988-400895	19880413
ES 2053779	T3	19940801	ES 1988-400895	19880413
AU 8814611	A1	19881020	AU 1988-14611	19880414
AU 606146	B2	19910131		
CN 88102139	A	19881026	CN 1988-102139	19880414
CN 1022411	B	19931013		
US 5049667	A	19910917	US 1989-421592	19891016
US 5417960	A	19950523	US 1994-191461	19940203

PRIORITY APPLN. INFO.:
FR 1987-5288 19870414
EP 1988-400895 19880413
US 1988-181056 19880413
FR 1988-13585 19881014
US 1989-421592 19891016
US 1991-730050 19910715

L8 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)
INDEX TERM: 78-90-0, 1,2-Diaminopropane 98-59-9, Tosyl chloride 110-97-4, Diisopropanolamine 111-42-2, reactions 141-52-6, Sodium ethylate 2984-50-1, 1,2-Epoxy octane 4439-20-7 6018-55-9, 2,3-Diaminopropionic acid hydrochloride 32503-27-8, Tetrabutylammonium hydrogen sulfate 56234-52-7 119929-12-3
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in complex prepn. for medical imaging agents)

L8 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)
ABSTRACT:
N-Contg. macrocycles are prepd. which are useful as ligands for complexes for NMR imaging and x-ray radiol. (no data). 2,6-Dimethyl-1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid was prepd., as was the methylglucamine salt of the Gd complex of the macrocycle.

SUPPL. TERM: nitrogen macrocycle ligand medical imaging; tomog NMR imaging agent; radiog imaging agent
INDEX TERM: Radiography
(macrocyclic complex prepn. for imaging agents for)
INDEX TERM: Tomography
(NMR, macrocyclic complex prepn. for imaging agents for)
INDEX TERM: Transition metals, compounds
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(macrocyclic compd. complexes, prepn. of, for complex prepn. for medical imaging agents)
INDEX TERM: Rare earth metals, compounds
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(macrocyclic-compd. complexes, prepn. of, for complex prepn. for medical imaging agents)
INDEX TERM: Macrocyclic compounds
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(rare earth metal complexes, prepn. of, for complex prepn. for medical imaging agents)
INDEX TERM: Macrocyclic compounds
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(transition metal complexes, prepn. of, for complex prepn. for medical imaging agents)
INDEX TERM: 16695-22-0P 56234-52-7P 74461-30-6P 89990-51-2P 119928-90-4P 119928-91-5P 119928-92-6P 119928-93-7P 119928-94-8P 119928-95-9P 119928-96-0P 119928-97-1P 119928-98-2P 119928-99-3P 119929-00-9P 119929-01-0P 119929-02-1P 119929-03-2P 119929-04-3P 119929-05-4P 119929-06-5P 119929-07-6P 119929-08-7P 119929-09-8P 119929-10-1P 119929-11-2P 119929-12-3P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, in complex prepn. for medical imaging agents)
INDEX TERM: 120001-37-8P 121843-19-4P 121843-20-7P 121843-21-8P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as medical imaging agent)
INDEX TERM: 7429-91-6DP, Dysprosium, macrocycle complexes
7439-89-6DP,
Iron, macrocycle complexes 7439-92-1DP, Lead, macrocycle complexes 7439-96-5DP, Manganese, macrocycle complexes 7440-39-3DP, Barium, macrocycle complexes 7440-46-2DP, Cesium, macrocycle complexes 7440-53-1DP, Europium, macrocycle complexes 7440-54-2DP, Gadolinium, macrocycle complexes 7440-69-9DP, Bismuth, macrocycle complexes 119928-83-5P 119928-84-6P 119928-85-7P 119928-86-8P 119928-87-9P 119928-88-0P 119928-89-1P 119929-12-3P 119989-35-4P 120001-37-8P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for complex prepn. for medical imaging agents)

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L9            1 EP374501/PN

=> d iall
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L9 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:574644 HCAPLUS
DOCUMENT NUMBER: 115:174644
TITLE: Radionuclide complexes as bone marrow suppressing agents
INVENTOR(S): Simon, Jaime; Garlich, Joseph R.; Wilson, David A.; McMillan, Kenneth
PATENT ASSIGNEE(S): Dow Chemical Co., USA
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K043-00
CLASSIFICATION: 1-6 (Pharmacology)
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 374501	A1	19900627	EP 1989-121564	19891121 <--
EP 374501	B1	19930804		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL				
US 4882142	A	19891121	US 1988-284875	19881219
US 4976950	A	19901211	US 1989-435096	19891113
CA 2003326	AA	19900619	CA 1989-2003326	19891120
CA 2003326	C	19990119		
DK 8905827	A	19900620	DK 1989-5827	19891120
IL 92373	A1	19950831	IL 1989-92373	19891120
JP 02237936	A2	19900920	JP 1989-300943	19891121
JP 2795934	B2	19980910		
ZA 8908866	A	19910731	ZA 1989-8866	19891121
AT 92339	E	19930815	AT 1989-121564	19891121
AU 8945440	A1	19900621	AU 1989-45440	19891122
AU 625644	B2	19920716		

PRIORITY APPLN. INFO.: US 1988-284875 19881219
EP 1989-121564 19891121

ABSTRACT:
Bone marrow is suppressed by the administration of 153Sm, 159Gd, 166Ho or 90Y complexes of aminophosphonic acid ligand(s) contg. the 1,4,7,10-tetraazacyclododecane moiety. A refluxing mixt. of 3.48 g 1,4,7,10-tetraazacyclodecane, 14 mL water, 17.2 mL conc. HCl and 7.2 g H3PO4 was treated with 13 g 37% HCHO, to give 1,4,7,10-tetraazacyclododecanetetramethylenephospho nic acid (DOTMP). This was treated with a 90YCl3 soln. in HCl, followed by pH adjustment to 7.5 (NaOH) to give 90Y-DOTMP. 90Y-DOTMP (1 mCi), injected i.v. into rats decreased the white blood cell count. The complexes may be used in the treatment of leukemia, lymphoma, myeloma, Hodgkin's disease, sickle cell anemia or thalassemia. The complexes may be used in conjunction with known chemotherapeutic agents.

SUPPL. TERM: radionuclide tetraazacyclododecane bone marrow; cancer radionuclide tetraazacyclododecane
INDEX TERM: Bone marrow
(suppression of, with radionuclide complexes of tetraazacyclododecanetetramethylenephosphonic acid, in

treatment of cancer and genetic diseases)
INDEX TERM: Neoplasm inhibitors
(Hodgkin's disease, radionuclide complexes of tetraazacyclododecanetetramethylephosphonic acid)
INDEX TERM: Radioelements, compounds
ROLE: BIOL (Biological study)
(complexes, with tetraazacyclododecanetetramethylenephosp honic acid, in treatment of cancer and genetic diseases)
INDEX TERM: Neoplasm inhibitors
(leukemia, radionuclide complexes of tetraazacyclododecanetetramethylephosphonic acid)
INDEX TERM: Neoplasm inhibitors
(lymphoma, radionuclide complexes of tetraazacyclododecanetetramethylephosphonic acid)
INDEX TERM: Neoplasm inhibitors
(myeloma, radionuclide complexes of tetraazacyclododecanetetramethylephosphonic acid)
INDEX TERM: 12064-62-9, Gadolinium oxide
ROLE: PROC (Process)
(irradn. of, for Gadolinium-159 prodn.)
INDEX TERM: 68052-85-7, Samarium oxide (152Sm2O3)
ROLE: PROC (Process)
(irradn. of, for Samarium-153 prodn.)
INDEX TERM: 1314-36-9, Yttrium trioxide, biological studies
ROLE: BIOL (Biological study)
(irradn. of, for Yttrium-90 prodn.)
INDEX TERM: 12055-62-8, biological studies
ROLE: BIOL (Biological study)
(irradn. of, for holmium-166 prodn.)
INDEX TERM: 10098-91-6DP, Yttrium-90, complex with tetraazacyclododecanetetramethylenephosphonic acid
13967-65-2DP, Holmium-166, complex with tetraazacyclododecanetetramethylenephosphonic acid
14041-42-0DP, Gadolinium-159, complex with tetraazacyclododecanetetramethylenephosphonic acid
15766-00-4DP, Samarium-153, complex with tetraazacyclododecanetetramethylenephosphonic acid
91987-74-5DP, complexes with radionuclides
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as bone marrow-suppressing agent, for treatment of cancer and genetic diseases)
INDEX TERM: 294-90-6, 1,4,7,10-Tetraazacyclododecane
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with phosphoric acid and formaldehyde)
INDEX TERM: 13598-36-2, Phosphorous acid
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with tetraazacyclododecane and formaldehyde)
INDEX TERM: 10294-56-1, Phosphorous acid, reactions
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with tetraazacyclododecane formaldehyde)
INDEX TERM: 50-00-0, Formaldehyde, reactions
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with tetraazadodecane phosphoric acid)

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                (EP374501/PN)

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L10 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:574644 HCAPLUS
DOCUMENT NUMBER: 115:174644
TITLE: Radionuclide complexes as bone marrow suppressing agents
INVENTOR(S): Simon, Jaime; Garlich, Joseph R.; Wilson, David A.; McMillan, Kenneth
PATENT ASSIGNEE(S): Dow Chemical Co., USA
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K043-00
CLASSIFICATION: 1-6 (Pharmacology)
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 374501	A1	19900627	EP 1989-121564	19891121 <--
EP 374501	B1	19930804		
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US 4882142	A	19891121	US 1988-284875	19881219
US 4976950	A	19901211	US 1989-435096	19891113
CA 2003326	AA	19900619	CA 1989-2003326	19891120
CA 2003326	C	19990119		
DK 8905827	A	19900620	DK 1989-5827	19891120
IL 92373	A1	19950831	IL 1989-92373	19891120
JP 02237936	A2	19900920	JP 1989-300943	19891121
JP 2795934	B2	19980910		
ZA 8908866	A	19910731	ZA 1989-8866	19891121
AT 92339	E	19930815	AT 1989-121564	19891121
AU 8945440	A1	19900621	AU 1989-45440	19891122
AU 625644	B2	19920716		
PRIORITY APPLN. INFO.:			US 1988-284875	19881219
			EP 1989-121564	19891121

ABSTRACT:
Bone marrow is suppressed by the administration of 153Sm, 159Gd, 166Ho or 90Y complexes of aminophosphonic acid ligand(s) contg. the 1,4,7,10-tetraazacyclododecane moiety. A refluxing mixt. of 3.48 g 1,4,7,10-tetraazacyclodecane, 14 mL water, 17.2 mL conc. HCl and 7.2 g H3PO4 was treated
with 13 g 37% HCHO, to give
1,4,7,10-tetraazacyclododecanetetramethylenephospho
nic acid (DOTMP). This was treated with a 90YCl3 soln. in HCl, followed by pH adjustment to 7.5 (NaOH) to give 90Y-DOTMP. 90Y-DOTMP (1 mCi), injected i.v. into rats decreased the white blood cell count. The complexes may be used in the treatment of leukemia, lymphoma, myeloma, Hodgkin's disease, sickle cell anemia or thalassemia. The complexes may be used in conjunction with known chemotherapeutic agents.

SUPPL. TERM: radionuclide tetraazacyclododecane bone marrow; cancer radionuclide tetraazacyclododecane
INDEX TERM: Bone marrow
(suppression of, with radionuclide complexes of tetraazacyclododecanetetramethylenephosphonic acid, in

L10 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)

L10 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)
treatment of cancer and genetic diseases)
INDEX TERM: Neoplasm inhibitors
(Hodgkin's disease, radionuclide complexes of tetraazacyclododecanetetramethylephosphonic acid)
INDEX TERM: Radioelements, compounds
ROLE: BIOL (Biological study)
(complexes, with
tetraazacyclododecanetetramethylenephosp
honic acid, in treatment of cancer and genetic diseases)
INDEX TERM: Neoplasm inhibitors
(leukemia, radionuclide complexes of tetraazacyclododecanetetramethylephosphonic acid)
INDEX TERM: Neoplasm inhibitors
(lymphoma, radionuclide complexes of tetraazacyclododecanetetramethylephosphonic acid)
INDEX TERM: Neoplasm inhibitors
(myeloma, radionuclide complexes of tetraazacyclododecanetetramethylephosphonic acid)
INDEX TERM: 12064-62-9, Gadolinium oxide
ROLE: PROC (Process)
(irradn. of, for Gadolinium-159 prodn.)
INDEX TERM: 68052-85-7, Samarium oxide (152Sm2O3)
ROLE: PROC (Process)
(irradn. of, for Samarium-153 prodn.)
INDEX TERM: 1314-36-9, Yttrium trioxide, biological studies
ROLE: BIOL (Biological study)
(irradn. of, for Yttrium-90 prodn.)
INDEX TERM: 12055-62-8, biological studies
ROLE: BIOL (Biological study)
(irradn. of, for holmium-166 prodn.)
INDEX TERM: 10098-91-6DP, Yttrium-90, complex with tetraazacyclododecanetetramethylenephosphonic acid
13967-65-2DP, Holmium-166, complex with tetraazacyclododecanetetramethylenephosphonic acid
14041-42-0DP, Gadolinium-159, complex with tetraazacyclododecanetetramethylenephosphonic acid
15766-00-4DP, Samarium-153, complex with tetraazacyclododecanetetramethylenephosphonic acid
91987-74-5DP, complexes with radionuclides
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as bone marrow-suppressing agent, for treatment of cancer and genetic diseases)
INDEX TERM: 294-90-6, 1,4,7,10-Tetraazacyclododecane
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with phosphoric acid and formaldehyde)
INDEX TERM: 13598-36-2, Phosphorous acid
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with tetraazacyclododecane and formaldehyde)
INDEX TERM: 10294-56-1, Phosphorous acid, reactions
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with tetraazacyclododecane formaldehyde)
INDEX TERM: 50-00-0, Formaldehyde, reactions
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with tetraazadodecane phosphoric acid)

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E4            1      EP382583/PN
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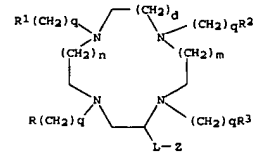
L11 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:122706 HCAPLUS
DOCUMENT NUMBER: 114:122706
TITLE: Preparation of tetraphosphinate-substituted tetraaza macrocycles for use as antitumor or imaging agents
INVENTOR(S): Parker, David; Eaton, Michael Anthony William
PATENT ASSIGNEE(S): Celltech Ltd., UK
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07F009-6524
SECONDARY: A61K031-675
CLASSIFICATION: 29-7 (Organometallic and Organometalloidal Compounds)
Section cross-reference(s): 1, 8, 28, 78
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 382582	A1	19900816	EP 1990-301477	19900212 <--
EP 382582	B1	19950419		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL				
CA 2026322	AA	19900811	CA 1990-2026322	19900212
WO 9009388	A1	19900823	WO 1990-GB231	19900212
W: AU, CA, JP, US				
AU 9050436	A1	19900905	AU 1990-50436	19900212
AU 633877	B2	19930211		
JP 03504608	T2	19911009	JP 1990-503007	19900212
AT 121412	E	19950515	AT 1990-301477	19900212
US 5342936	A	19940830	US 1992-964117	19921002

PRIORITY APPLN. INFO.: GB 1989-3023 19890210
WO 1990-GB231 19900212
US 1990-601705 19901030
US 1992-826669 19920129
OTHER SOURCE(S): MARPAT 114:122706
GRAPHIC IMAGE:

L11 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)



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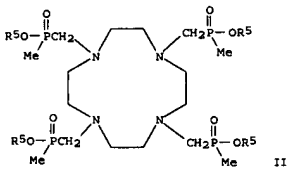

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ABSTRACT:
Title compds. I [m, n, d = 0-3; q = 0-6; R-R3 = H, P(O)(XH)R4 (.gtoreq.1 R .noteq. H); X = O, S; R4 = H, alkyl, alkoxy; L = bond or divalent group; Z = H or reactive functional group] and their salts and complexes were prepd. as antitumor and/or imaging agents (no data). For example, 1,4,7,10-tetraazacyclododecane was condensed with MeP(OEt)2 and paraformaldehyde to give
tetraphosphinate ester II (R5 = Et), which was hydrolyzed in refluxing HCl to give II (R5 = H). This acid formed complexes with Y, Gd, and 90Y. The latter was prepd. in 82% radiolabeling yield, and was stable in aq. buffer (pH 6.8) at
298 K in the presence of a 500-fold excess of DTPA for 72 h. Three addnl. I (Z
= NH2 or deriv.) were also prepd.

SUPPL. TERM: tetraaza macrocycle phosphinate antitumor imaging; radiolabel macrocycle yttrium gadolinium complex
INDEX TERM: Neoplasm inhibitors
(tetraaza macrocycles and complexes)
INDEX TERM: Tomography
(contrast agents, tetraaza macrocycle complexes)
INDEX TERM: Crown compounds
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(imines, prepn. of, as antitumor and/or imaging agents)
INDEX TERM: 96755-84-9
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(amidation of, with (aminobutyl)tetraazacyclododecane deriv.)

L11 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)
INDEX TERM: 107-15-3, 1,2-Ethanediamine, reactions
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(amidation of, with Me diaminohexanoate)
INDEX TERM: 13515-95-2
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(amidation of, with ethylenediamine)
INDEX TERM: 98-88-4, Benzoyl chloride
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(benzoylation by, of triaminoazanonane)
INDEX TERM: 74-95-3, Methylene bromide
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with diethoxymethylphosphine)
INDEX TERM: 30525-89-4, Paraformaldehyde
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with diethoxymethylphosphine and tetraazacyclododecane deriv.)
INDEX TERM: 15715-41-0, Diethoxymethylphosphine
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with methylene bromide, or paraformaldehyde and tetraazacyclododecane derivs.)
INDEX TERM: 294-90-6, 1,4,7,10-Tetraazacyclododecane
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with paraformaldehyde and diethoxymethylphosphine)
INDEX TERM: 16695-22-0
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation of, with bis(tosylamino)tosylbenzamido azanonane)
INDEX TERM: 132446-32-3P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and alkylation by, of tetraazacyclododecane deriv.)
INDEX TERM: 132446-36-7P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and alkylation of, by methyl(bromomethyl)phosphinate)
INDEX TERM: 123107-77-7P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and benzoylation of)
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(prepn. and borane redn. of)
INDEX TERM: 125552-36-5P
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(prepn. and cyclocondensation of, with tosylated diethanolamine)
INDEX TERM: 123107-80-2P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and detosylation of)
INDEX TERM: 123107-78-8P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and tosylation of)

L11 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)
INDEX TERM: 132250-24-9P 132250-25-0P 132250-26-1P 132250-27-2P
132250-28-3P 132446-31-2P 132446-33-4P 132446-34-5P
132446-35-6P 132470-81-6P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antitumor and/or imaging agent)
INDEX TERM: 98-59-9, Tosyl chloride
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(tosylation by, of diaminobenzamidodeoxyglucopyranosidylt rialkylazanonane)

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L13 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:122706 HCAPLUS
DOCUMENT NUMBER: 114:122706
TITLE: Preparation of tetraphosphinate-substituted tetraaza macrocycles for use as antitumor or imaging agents
INVENTOR(S): Parker, David; Eaton, Michael Anthony William
PATENT ASSIGNEE(S): Celltech Ltd., UK
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07F009-6524
SECONDARY: A61K031-675
CLASSIFICATION: 29-7 (Organometallic and Organometalloidal Compounds)
Section cross-reference(s): 1, 8, 28, 78
FAMILY ACC. NUM. COUNT: 1
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W: AU, CA, JP, US				
AU 9050436	A1	19900905	AU 1990-50436	19900212
AU 633877	B2	19930211		
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AT 121412	E	19950515	AT 1990-301477	19900212
US 5342936	A	19940830	US 1992-964117	19921002

PRIORITY APPLN. INFO.: GB 1989-3023 19890210
WO 1990-GB231 19900212
US 1990-601705 19901030
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OTHER SOURCE(S): MARPAT 114:122706
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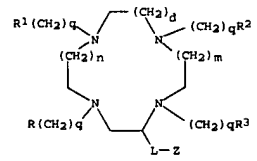
L13 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)



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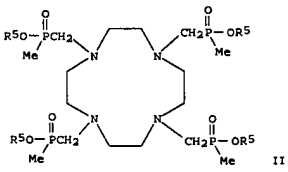

II

ABSTRACT:
Title compds. I [m, n, d = 0-3; q = 0-6; R-R3 = H, P(O)(XH)R4 (.gtoreq.1 R .noteq. H); X = O, S; R4 = H, alkyl, alkoxy; L = bond or divalent group; Z = H or reactive functional group] and their salts and complexes were prepd. as antitumor and/or imaging agents (no data). For example, 1,4,7,10-tetraazacyclododecane was condensed with MeP(OEt)2 and paraformaldehyde to give
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298 K in the presence of a 500-fold excess of DTPA for 72 h. Three addnl. I (Z
= NH2 or deriv.) were also prepd.

SUPPL. TERM: tetraaza macrocycle phosphinate antitumor imaging; radiolabel macrocycle yttrium gadolinium complex
INDEX TERM: Neoplasm inhibitors
(tetraaza macrocycles and complexes)
INDEX TERM: Tomography
(contrast agents, tetraaza macrocycle complexes)
INDEX TERM: Crown compounds
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(imines, prepn. of, as antitumor and/or imaging agents)
INDEX TERM: 96755-84-9
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(amidation of, with (aminobutyl)tetraazacyclododecane deriv.)

L13 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)
INDEX TERM: 107-15-3, 1,2-Ethanediamine, reactions
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(amidation of, with Me diaminohexanoate)
INDEX TERM: 13515-95-2
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(amidation of, with ethylenediamine)
INDEX TERM: 98-88-4, Benzoyl chloride
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(benzoylation by, of triaminoazanonane)
INDEX TERM: 74-95-3, Methylene bromide
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with diethoxymethylphosphine)
INDEX TERM: 30525-89-4, Paraformaldehyde
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with diethoxymethylphosphine and tetraazacyclododecane derivs.)
INDEX TERM: 15715-41-0, Diethoxymethylphosphine
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with methylene bromide, or paraformaldehyde and tetraazacyclododecane derivs.)
INDEX TERM: 294-90-6, 1,4,7,10-Tetraazacyclododecane
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with paraformaldehyde and diethoxymethylphosphine)
INDEX TERM: 16695-22-0
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation of, with bis(tosylamino)tosylbenzamido azanonane)
INDEX TERM: 132446-32-3P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and alkylation by, of tetraazacyclododecane deriv.)
INDEX TERM: 132446-36-7P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and alkylation of, by methyl(bromomethyl)phosphinate)
INDEX TERM: 123107-77-7P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and benzoylation of)
INDEX TERM: 123107-76-6P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and borane redn. of)
INDEX TERM: 125552-36-5P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and cyclocondensation of, with tosylated diethanolamine)
INDEX TERM: 123107-80-2P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and detosylation of)
INDEX TERM: 123107-78-8P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and tosylation of)

L13 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)
INDEX TERM: 132250-24-9P 132250-25-0P 132250-26-1P 132250-27-2P
132250-28-3P 132446-31-2P 132446-33-4P 132446-34-5P
132446-35-6P 132470-81-6P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antitumor and/or imaging agent)
INDEX TERM: 98-59-9, Tosyl chloride
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(tosylation by, of diaminobenzamidodeoxyglucopyranosidylt rialkylazanonane)

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=> s ep0408701/pn
L14           1 EP0408701/PN
                (EP408701/PN)

=> d iall
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L14 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:95158 HCAPLUS
DOCUMENT NUMBER: 114:95158
TITLE: Preparation of macrocyclic aminophosphonic acid complexes of radionuclides as neoplasm inhibitors
INVENTOR(S): Simon, Jaime; Wilson, David A.; Garlich, Joseph R.; Troutner, David E.
PATENT ASSIGNEE(S): Dow Chemical Co., USA
SOURCE: Eur. Pat. Appl., 21 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K043-00
ADDITIONAL: C07F005-00
CLASSIFICATION: 1-6 (Pharmacology)
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
EP 375376	A2	19900627	EP 1989-313308	19891219	
EP 375376	A3	19910612			
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE					
US 5059412	A	19911022	US 1988-284876	19881219	
WO 9006776	A1	19900628	WO 1989-US5782	19891215	
W: AU, BR, DK, FI, HU, JP, KR, NO					
RW: AT, BE, CH, DE, ES, FR, GB, IT, LU, NL, SE					
AU 9048282	A1	19900710	AU 1990-48282	19891215	
AU 639899	B2	19930812			
EP 408701	A1	19910123	EP 1990-901464	19891215	<--
EP 408701	B1	19941012			
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE					
BR 8907255	A	19910312	BR 1989-7255	19891215	
HU 54897	A2	19910429	HU 1990-1163	19891215	
HU 207454	B	19930428			
JP 03502936	T2	19910704	JP 1990-501907	19891215	
ES 2061010	T3	19941201	ES 1990-901464	19891215	
JP 2515929	B2	19960710	JP 1989-501907	19891215	
CA 2005880	AA	19900619	CA 1989-2005880	19891218	
CA 2005880	C	19990105			
IL 92784	A1	19940826	IL 1989-92784	19891218	
AU 8947009	A1	19900621	AU 1989-47009	19891219	
CN 1046739	A	19901107	CN 1989-109819	19891219	
CN 1025983	B	19940928			
ZA 8909734	A	19910828	ZA 1989-9734	19891219	
DK 9001959	A	19900816	DK 1990-1959	19900816	
NO 9003632	A	19901017	NO 1990-3632	19900817	
NO 180434	B	19970113			
NO 180434	C	19970423			
AU 9350685	A1	19940224	AU 1993-50685	19931112	
AU 657641	B2	19950316			

PRIORITY APPLN. INFO.: US 1988-284876 A 19881219
US 1984-616985 B2 19840604
US 1985-738010 B2 19850528
US 1985-803376 B2 19851204
US 1987-50263 A2 19870514

L14 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)
antitumor agent prepn.)
INDEX TERM: 10294-56-1, Phosphorous acid, reactions
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with tetraazacyclododecane and formaldehyde
in antitumor prepn.)
INDEX TERM: 50-00-0, Formaldehyde, reactions
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with tetraazacyclododecane and phosphoric acid in antitumor prepn.)

L14 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)
WO 1989-US5782 A 19891215
OTHER SOURCE(S): MARPAT 114:95158
ABSTRACT:
153Sm, 159Gd, 166Ho, 177Lu, 90Y or 175Yb are complexes with macrocyclic aminophosphonic acids contg. the 1,4,7,10-tetraazacyclododecane moiety and having the N and P interconnected by (un)substituted alkylene. The complexes are useful in the treatment of bone-metastatic cancer. A refluxing mixt. of 3.48 g 1,4,7,10-tetraazacyclododecane, 17.2 mL conc. HCl, 7.2 g H3PO4 and 14 mL
water was treated with 13 g HCHO, to give 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetramethylphosphonic acid (DOTMP). This was complexed with 166Ho at pH 7-8, to give DOTMP-166Ho. Biodistribution studies of DOTMP-166Ho in rats showed strong accumulation in the bone.

SUPPL. TERM: radionuclide complex tetraazacyclododecane deriv anticancer;
bone cancer drug radionuclide complex
INDEX TERM: Radioelements, biological studies
ROLE: BIOL (Biological study)
(complexes with tetraazacyclododecanetetramethylphosphoni
c acid, for treatment of bone-marrow cancer)
INDEX TERM: Neoplasm inhibitors
(radionuclide complexes of tetraazacyclododecanetetrameth
ylphosphonic acid)
INDEX TERM: Bone, neoplasm
(metastasis, treatment of, with radionuclide complexes of
tetraazacyclodecanetetramethylphosphonic acid)
INDEX TERM: 10098-91-6DP, Yttrium-90, complex with tetraazacyclododecanetetramethylenephosphonic acid
13967-65-2DP, complex with tetraazacyclododecanetetramethyle
nephosphonic acid 14041-42-0DP, Gadolinium-159, complex with tetraazacyclododecanetetramethylenephosphonic acid
14041-44-2DP, Ytterbium-175, complex with tetraazacyclododecanetetramethylenephosphonic acid
14265-75-9DP, Lutetium-177, complex with tetraazacyclododecanetetramethylenephosphonic acid
29977-47-7DP, Samarium-158, complex with tetraazacyclododecanetetramethylenephosphonic acid
91987-74-5DP, complexes with radionuclides
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for treatment of bone cancer)
INDEX TERM: 39271-65-3, Yttrium chloride (90YCl3) 68052-85-7, Samarium
oxide (152Sm2O3) 132265-01-1, Holmium oxide (166Ho2O3)
132265-02-2, Gadolinium oxide (159Gd2O3)
ROLE: BIOL (Biological study)
(radionuclide complex of tetraazacyclododecane deriv. by,
for treatment of bone-marrow cancer)
INDEX TERM: 294-90-6, 1,4,7,10-Tetraazacyclododecane
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with formaldehyde and phosphoric acid in

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=> s ep0408701/pn
L15           1 EP0408701/PN
                (EP408701/PN)

=> d iall
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L15 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:95158 HCAPLUS
DOCUMENT NUMBER: 114:95158
TITLE: Preparation of macrocyclic aminophosphonic acid complexes of radionuclides as neoplasm inhibitors
INVENTOR(S): Simon, Jaime; Wilson, David A.; Garlich, Joseph R.; Troutner, David E.
PATENT ASSIGNEE(S): Dow Chemical Co., USA
SOURCE: Eur. Pat. Appl., 21 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K043-00
ADDITIONAL: C07F005-00
CLASSIFICATION: 1-6 (Pharmacology)
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
EP 375376	A2	19900627	EP 1989-313308	19891219	
EP 375376	A3	19910612			
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE					
US 5059412	A	19911022	US 1988-284876	19881219	
WO 9006776	A1	19900628	WO 1989-US5782	19891215	
W: AU, BR, DK, FI, HU, JP, KR, NO					
RW: AT, BE, CH, DE, ES, FR, GB, IT, LU, NL, SE					
AU 9048282	A1	19900710	AU 1990-48282	19891215	
AU 639899	B2	19930812			
EP 408701	A1	19910123	EP 1990-901464	19891215	<--
EP 408701	B1	19941012			
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE					
BR 8907255	A	19910312	BR 1989-7255	19891215	
HU 54897	A2	19910429	HU 1990-1163	19891215	
HU 207454	B	19930428			
JP 03502936	T2	19910704	JP 1990-501907	19891215	
ES 2061010	T3	19941201	ES 1990-901464	19891215	
JP 2515929	B2	19960710	JP 1989-501907	19891215	
CA 2005880	AA	19900619	CA 1989-2005880	19891218	
CA 2005880	C	19990105			
IL 92784	A1	19940826	IL 1989-92784	19891218	
AU 8947009	A1	19900621	AU 1989-47009	19891219	
CN 1046739	A	19901107	CN 1989-109819	19891219	
CN 1025983	B	19940928			
ZA 8909734	A	19910828	ZA 1989-9734	19891219	
DK 9001959	A	19900816	DK 1990-1959	19900816	
NO 9003632	A	19901017	NO 1990-3632	19900817	
NO 180434	B	19970113			
NO 180434	C	19970423			
AU 9350685	A1	19940224	AU 1993-50685	19931112	
AU 657641	B2	19950316			

PRIORITY APPLN. INFO.: US 1988-284876 A 19881219
US 1984-616985 B2 19840604
US 1985-738010 B2 19850528
US 1985-803376 B2 19851204
US 1987-50263 A2 19870514

L15 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)
antitumor agent prepn.)
INDEX TERM: 10294-56-1, Phosphorous acid, reactions
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with tetraazacyclododecane and formaldehyde
in antitumor prepn.)
INDEX TERM: 50-00-0, Formaldehyde, reactions
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with tetraazacyclododecane and phosphoric acid in antitumor prepn.)

L15 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)
WO 1989-US5782 A 19891215
OTHER SOURCE(S): MARPAT 114:95158
ABSTRACT:
153Sm, 159Gd, 166Ho, 177Lu, 90Y or 175Yb are complexes with macrocyclic aminophosphonic acids contg. the 1,4,7,10-tetraazacyclododecane moiety and having the N and P interconnected by (un)substituted alkylene. The complexes are useful in the treatment of bone-metastatic cancer. A refluxing mixt. of 3.48 g 1,4,7,10-tetraazacyclododecane, 17.2 mL conc. HCl, 7.2 g H3PO4 and 14 mL
water was treated with 13 g HCHO, to give 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetramethylphosphonic acid (DOTMP). This was complexed with 166Ho at pH 7-8, to give DOTMP-166Ho. Biodistribution studies of DOTMP-166Ho in rats showed strong accumulation in the bone.

SUPPL. TERM: radionuclide complex tetraazacyclododecane deriv anticancer;
bone cancer drug radionuclide complex
INDEX TERM: Radioelements, biological studies
ROLE: BIOL (Biological study)
(complexes with tetraazacyclododecanetetramethylphosphoni
c acid, for treatment of bone-marrow cancer)
INDEX TERM: Neoplasm inhibitors
(radionuclide complexes of tetraazacyclododecanetetrameth
ylphosphonic acid)
INDEX TERM: Bone, neoplasm
(metastasis, treatment of, with radionuclide complexes of
tetraazacyclodecanetetramethylphosphonic acid)
INDEX TERM: 10098-91-6DP, Yttrium-90, complex with tetraazacyclododecanetetramethylenephosphonic acid
13967-65-2DP, complex with tetraazacyclododecanetetramethyle
nephosphonic acid 14041-42-0DP, Gadolinium-159, complex with tetraazacyclododecanetetramethylenephosphonic acid
14041-44-2DP, Ytterbium-175, complex with tetraazacyclododecanetetramethylenephosphonic acid
14265-75-9DP, Lutetium-177, complex with tetraazacyclododecanetetramethylenephosphonic acid
29977-47-7DP, Samarium-158, complex with tetraazacyclododecanetetramethylenephosphonic acid
91987-74-5DP, complexes with radionuclides
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for treatment of bone cancer)
INDEX TERM: 39271-65-3, Yttrium chloride (90YCl3) 68052-85-7, Samarium
oxide (152Sm2O3) 132265-01-1, Holmium oxide (166Ho2O3) 132265-02-2, Gadolinium oxide (159Gd2O3)
ROLE: BIOL (Biological study)
(radionuclide complex of tetraazacyclododecane deriv. by,
for treatment of bone-marrow cancer)
INDEX TERM: 294-90-6, 1,4,7,10-Tetraazacyclododecane
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with formaldehyde and phosphoric acid in

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**** START OF FIELD ****
E2            1     0 20180363/PN
E3            0 --> 0411941/PN
E4            1     AN6414144/PN
E5            1     AP1000/PN
E6            1     AP1001/PN
E7            1     AP1002/PN
E8            1     AP1004/PN
E9            1     AP1005/PN
E10           1     AP1006/PN
E11           1     AP1007/PN
E12           1     AP1009/PN

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E1            1     EP411937/PN
E2            1     EP411938/PN
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E8            1     EP411949/PN
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E10           1     EP411952/PN
E11           1     EP411957/PN
E12           1     EP411968/PN

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L16 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1990:572351 HCAPLUS
DOCUMENT NUMBER: 113:172351
TITLE: Method for purifying aminomethylenephosphonic acids for pharmaceutical use
INVENTOR(S): Garlich, Joseph R.; Simon, Jaime; Masterson, Tipton T.
PATENT ASSIGNEE(S): Dow Chemical Co., USA
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07F009-38
SECONDARY: C07F009-66
US PATENT CLASSIF.: 540474000
CLASSIFICATION: 29-7 (Organometallic and Organometalloidal Compounds)
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4937333	A	19900626	US 1989-389441	19890804
CA 2020950	AA	19910205	CA 1990-2020950	19900711
ZA 9005564	A	19920325	ZA 1990-5564	19900716
IL 95094	A1	19950526	IL 1990-95094	19900716
IL 110861	A1	19990714	IL 1990-110861	19900716
JP 03066697	A2	19910322	JP 1990-194121	19900724
JP 2922263	B2	19990719		
BR 9003694	A	19910903	BR 1990-3694	19900724
CN 1049351	A	19910220	CN 1990-104982	19900728
CN 1024196	B	19940413		
CN 1091744	A	19940907	CN 1993-108500	19900728
CN 1031191	B	19960306		
SK 279107	B6	19980603	SK 1990-3796	19900731
CZ 290556	B6	20020814	CZ 1990-3796	19900731
EP 411941	A2	19910206	EP 1990-308524	19900802 <--
EP 411941	A3	19920415		
EP 411941	B1	19960717		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
RO 105967	B1	19930130	RO 1990-145690	19900802
AT 140459	E	19960815	AT 1990-308524	19900802
ES 2090105	T3	19961016	ES 1990-308524	19900802
NO 9003419	A	19910205	NO 1990-3419	19900803
NO 178196	B	19951030		
NO 178196	C	19960207		
HU 54698	A2	19910328	HU 1990-4890	19900803
HU 205128	B	19920330		
DD 297414	A5	19920109	DD 1990-343237	19900803
SU 1838321	A3	19930830	SU 1990-4830923	19900803
PL 164908	B1	19941031	PL 1990-300181	19900803
PL 166453	B1	19950531	PL 1990-286349	19900803
AU 9060237	A1	19910207	AU 1990-60237	19900806
AU 634267	B2	19930218		
LV 10718	B	19960420	LV 1993-934	19930630
NO 9400643	A	19910205	NO 1994-643	19940224
NO 9502161	A	19910205	NO 1995-2161	19950531

L16 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)

L16 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)

NO 179451	B	19960701			
NO 179451	C	19961009			
FI 9504391	A	19950918	FI 1995-4391		19950918
NO 9604191	A	19901017	NO 1996-4191		19961003
NO 9700653	A	19910205	NO 1997-653		19970212
PRIORITY APPLN. INFO.:			US 1988-284876	A	19881219
			US 1989-389441	A	19890804
			WO 1989-US5782	W	19891215
			IL 1990-95094	A3	19900716
			FI 1990-3864	A	19900803
			NO 1990-3419	A	19900803
			NO 1990-3632	A	19900817

ABSTRACT:
(H2O3PCH2)2NCH2CH2N(CH2PO3H2)2 (I) and 1,4,7,10-tetraazacyclododecane 1,4,7,10-tetra(methylenephosphonic acid) (II) were purified by 1) dissoln. in aq. base (NH3), 2) addn. of the soln. to an acid soln. (HCl) at elevated temp.,
3) cooling of the resulting soln. to ppt. I or II, and 4) filtration and washing with H2O. Thus, a mixt. of H3PO3, H2NCH2CH2NH2.2HCl, and conc HCl at 100.degree. was treated over 22-24 h with 37% aq. H2CO; the mixt. was refluxed an addnl. 4 h and vacuum filtered at boiling to give I contg <1% impurities. The above I in concd. aq. NH3 was poured into 3 M HCl at 100.degree. and the mixt. was brought to reflux for 30 min and then stirred 21 h at 43.degree. followed by filtration and washing with H2O to give I contg. .apprx.0.6% impurities.

SUPPL. TERM: tetraazacyclododecane tetramethylene phosphonate prepn purifn; ethylenediamine tetramethylenephosphonate prepn purifn
INDEX TERM: Chelating agents
(poly(aminomethylaminephosphonic acid), high purity, prepn. of, for use in imaging and radiopharmaceutical agents)
INDEX TERM: 13598-36-2, Phosphorous acid
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with ethylenediamine and formaldehyde)
INDEX TERM: 50-00-0, Formaldehyde, reactions
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with ethylenediamine and phosphorous acid)
INDEX TERM: 333-18-6, Ethylenediamine dihydrochloride
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with phosphorous acid and formaldehyde)
INDEX TERM: 294-90-6, 1,4,7,10-Tetraazacyclododecane
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(phosphonomethylation of)
INDEX TERM: 1429-50-1P 91987-74-5P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and purifn. of)
INDEX TERM: 7647-01-0P, Hydrochloric acid, preparation
ROLE: PREP (Preparation)
(use of, in purifn. of alkylamine methylenephosphonates)
INDEX TERM: 1336-21-6, Ammonium hydroxide
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(use of, in purifn. of alkylamine methylenephosphonates)

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L17          1 EP0698029/PN
                (EP698029/PN)

=> d iall
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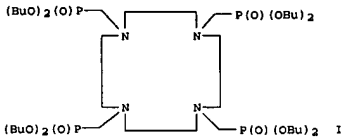
L17 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:380314 HCAPLUS
DOCUMENT NUMBER: 122:160930
TITLE: Process for the preparation of azamacrocyclic or acyclic aminophosphonate ester derivatives
INVENTOR(S): Kiefer, Garry E.
PATENT ASSIGNEE(S): Dow Chemical Co., USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07F009-65
CLASSIFICATION: 29-7 (Organometallic and Organometalloidal Compounds)
Section cross-reference(s): 28
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9426753	A1	19941124	WO 1994-US5134	19940504
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5714604	A	19980203	US 1993-65963	19930506
AU 9469086	A1	19941212	AU 1994-69086	19940504
AU 682190	B2	19970925		
EP 698029	A1	19960228	EP 1994-917333	19940504 <--
EP 698029	B1	19981104		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE				
HU 73142	A2	19960628	HU 1995-3175	19940504
CN 1125949	A	19960703	CN 1994-192530	19940504
CN 1042537	B	19990317		
JP 08510249	T2	19961029	JP 1994-525620	19940504
AT 172978	E	19981115	AT 1994-917333	19940504
ES 2123137	T3	19990101	ES 1994-917333	19940504
RO 115883	B1	20000728	RO 1995-1927	19940504
PL 180756	B1	20010430	PL 1994-311651	19940504
CZ 290993	B6	20021113	CZ 1995-2890	19940504
RU 2135507	C1	19990827	RU 1995-122389	19940505
ZA 9403158	A	19951106	ZA 1994-3158	19940506
LT 3713	B	19960226	LT 1994-1925	19940506
LV 10867	B	19960820	LV 1994-99	19940506
FI 9505281	A	19951220	FI 1995-5281	19951103
NO 9504439	A	19960105	NO 1995-4439	19951106

PRIORITY APPLN. INFO.: US 1993-65963 A 19930506
WO 1994-US5134 W 19940504

OTHER SOURCE(S): CASREACT 122:160930; MARPAT 122:160930
GRAPHIC IMAGE:

L17 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)



I

ABSTRACT:
A novel process for the prepn. of azamacrocyclic or acyclic aminophosphonate ester derivs., e.g., I, is disclosed. The process concerns the reaction of an appropriate azamacrocyclic or acyclic primary or secondary amine with trialkyl phosphites and paraformaldehyde.

SUPPL. TERM: azamacrocyclic aminophosphonate; phosphonate azamacrocyclic acyclic
INDEX TERM: 50-00-0, Formaldehyde, reactions 102-85-2, Tributyl phosphite 107-15-3, Ethylenediamine, reactions
121-45-9,
Trimethyl phosphite 122-52-1, Triethyl phosphite
294-90-6, Cyclen 923-99-9, Tripropyl phosphite
78668-34-5 115078-43-8 161034-95-3
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of azamacrocyclic or acyclic aminophosphonates)
INDEX TERM: 154882-98-1P 160982-00-3P 160982-01-4P 160982-02-5P
161034-92-0P 161034-93-1P 161034-96-4P 161034-97-5P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of azamacrocyclic or acyclic aminophosphonates)
INDEX TERM: 1429-50-1P 137837-23-1P 160982-05-8P 160982-06-9P
160982-07-0P 161034-88-4P 161034-91-9P 161034-99-7P
161035-00-3P 161189-92-0P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of azamacrocyclic or acyclic aminophosphonates)

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E7            1     EP698033/PN
E8            1     EP698034/PN
E9            1     EP698035/PN
E10           1     EP698036/PN
E11           1     EP698037/PN
E12           1     EP698038/PN

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L18           1 EP698029/PN

=> d iall
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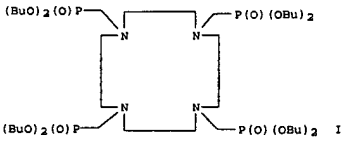
L18 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:380314 HCAPLUS
DOCUMENT NUMBER: 122:160930
TITLE: Process for the preparation of azamacrocyclic or acyclic aminophosphonate ester derivatives
INVENTOR(S): Kiefer, Garry E.
PATENT ASSIGNEE(S): Dow Chemical Co., USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07F009-65
CLASSIFICATION: 29-7 (Organometallic and Organometalloidal Compounds)
Section cross-reference(s): 28
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9426753	A1	19941124	WO 1994-US5134	19940504
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5714604	A	19980203	US 1993-65963	19930506
AU 9469086	A1	19941212	AU 1994-69086	19940504
AU 682190	B2	19970925		
EP 698029	A1	19960228	EP 1994-917333	19940504 <--
EP 698029	B1	19981104		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE				
HU 73142	A2	19960628	HU 1995-3175	19940504
CN 1125949	A	19960703	CN 1994-192530	19940504
CN 1042537	B	19990317		
JP 08510249	T2	19961029	JP 1994-525620	19940504
AT 172978	E	19981115	AT 1994-917333	19940504
ES 2123137	T3	19990101	ES 1994-917333	19940504
RO 115883	B1	20000728	RO 1995-1927	19940504
PL 180756	B1	20010430	PL 1994-311651	19940504
CZ 290993	B6	20021113	CZ 1995-2890	19940504
RU 2135507	C1	19990827	RU 1995-122389	19940505
ZA 9403158	A	19951106	ZA 1994-3158	19940506
LT 3713	B	19960226	LT 1994-1925	19940506
LV 10867	B	19960820	LV 1994-99	19940506
FI 9505281	A	19951220	FI 1995-5281	19951103
NO 9504439	A	19960105	NO 1995-4439	19951106

PRIORITY APPLN. INFO.: US 1993-65963 A 19930506
WO 1994-US5134 W 19940504
OTHER SOURCE(S): CASREACT 122:160930; MARPAT 122:160930
GRAPHIC IMAGE:

L18 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)



I

ABSTRACT:
A novel process for the prepn. of azamacrocyclic or acyclic aminophosphonate ester derivs., e.g., I, is disclosed. The process concerns the reaction of an appropriate azamacrocyclic or acyclic primary or secondary amine with trialkyl phosphites and paraformaldehyde.

SUPPL. TERM: azamacrocyclic aminophosphonate; phosphonate azamacrocyclic acyclic
INDEX TERM: 50-00-0, Formaldehyde, reactions 102-85-2, Tributyl phosphite 107-15-3, Ethylenediamine, reactions
121-45-9,
Trimethyl phosphite 122-52-1, Triethyl phosphite
294-90-6, Cyclen 923-99-9, Tripropyl phosphite
78668-34-5 115078-43-8 161034-95-3
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of azamacrocyclic or acyclic aminophosphonates)
INDEX TERM: 154882-98-1P 160982-00-3P 160982-01-4P 160982-02-5P
161034-92-0P 161034-93-1P 161034-96-4P 161034-97-5P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of azamacrocyclic or acyclic aminophosphonates)
INDEX TERM: 1429-50-1P 137837-23-1P 160982-05-8P 160982-06-9P
160982-07-0P 161034-88-4P 161034-91-9P 161034-99-7P
161035-00-3P 161189-92-0P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of azamacrocyclic or acyclic aminophosphonates)

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E2            1      EP972527/PN
E3            2 --> EP972528/PN
E4            1      EP972529/PN
E5            1      EP97253/PN
E6            1      EP972530/PN
E7            1      EP972538/PN
E8            1      EP97254/PN
E9            1      EP972543/PN
E10           1      EP972551/PN
E11           1      EP972552/PN
E12           1      EP972553/PN

=> s e3
L19           2 EP972528/PN

=> d iall 1-
YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y
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L19 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:50043 HCAPLUS
DOCUMENT NUMBER: 132:104773
TITLE: Radioimmunoconjugate for use in human therapy and its preparation
INVENTOR(S): Benes, Ivan Friedrich; Bosslet, Klaus
PATENT ASSIGNEE(S): Switz.
SOURCE: Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
INT. PATENT CLASSIF.:
MAIN: A61K051-10
CLASSIFICATION: 8-9 (Radiation Biochemistry)
Section cross-reference(s): 15, 63
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 972528	A2	20000119	EP 1999-106013	19990325 <--
EP 972528	A3	20021009		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
DE 19813687	A1	19990930	DE 1998-19813687	19980327
DE 19911329	A1	20000921	DE 1999-19911329	19990315

PRIORITY APPLN. INFO.: DE 1998-19813687 A 19980327
DE 1999-19911329 A 19990315

ABSTRACT:
A conjugate of a monoclonal antibody to cells of the hematopoietic system with an .alpha.- or .beta.-emitter is useful for treatment of malignant hematopoietic diseases. Suitable .alpha.-emitters are 211At and 212Bi, and suitable .beta.-emitters are 90Y, 188Re, 186Re, 67Cu, 166Ho, and 153Sm; the radionuclide is bound to the antibody with or without use of a complexing agent. The radionuclide is not an I isotope. The monoclonal antibody may bind
e.g. to a surface antigen of granulocytes or granulocyte precursors or to .gtoreq.1 epitope of CD66. Thus, a purified anti-CD66 monoclonal antibody was subjected to partial reductive cleavage with 2-mercaptoethanol and lyophilized.
This antibody was labeled with 188Re by mixing with a soln. of freshly prepd. Na188ReO4 in the presence of tetra-Na 1,1,3,3-propanetetraphosphonate Sn(II) complex. This conjugate, when administered i.v. to patients with chronic myeloid leukemia at 100 mCi/wk, accumulated in the bone marrow and led to a high rate of destruction of endogenous hematopoietic stem cells and 100% acceptance of autologous or allogeneic bone marrow transplants.

SUPPL. TERM: radioimmunoconjugate hematopoietic disease treatment; monoclonal antibody radionuclide conjugate leukemia; radiotherapy bone marrow disease
INDEX TERM: Lymphoma
(B-cell, radiolabeled monoclonal antibody to; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: CD antigens
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(CD66, radiolabeled monoclonal antibody to; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Histocompatibility antigens
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(HLA-DR, HLA-DR-10.beta., radiolabeled monoclonal antibody to; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(Kaposi's sarcoma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(bladder carcinoma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Transplant and Transplantation
Transplant and Transplantation
(bone marrow; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Bladder
Bladder
Kidney, neoplasm
Lung, neoplasm
Mammary gland
Neck, anatomical
Neck, anatomical
Pancreas, neoplasm
Pancreas, neoplasm
Prostate gland
Stomach, neoplasm
Stomach, neoplasm
(carcinoma, inhibitors, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Lung, neoplasm
Lung, neoplasm
Mammary gland
Mammary gland
Prostate gland
Prostate gland
(carcinoma, inhibitors; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Lung, neoplasm
Mammary gland
Prostate gland
(carcinoma, metastasis, inhibitors; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(colon carcinoma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(colon carcinoma; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Intestine, neoplasm
(colon, carcinoma, inhibitors, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Intestine, neoplasm
Intestine, neoplasm
(colon, carcinoma, inhibitors; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Intestine, neoplasm
(colon, carcinoma, metastasis, inhibitors; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Intestine, neoplasm
(colorectal, carcinoma, inhibitors, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Hematopoiesis
(disorders; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Hematopoietic precursor cell
(granulocyte-macrophage, monoclonal antibody to, radiolabeled; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Blood vessel, neoplasm
Blood vessel, neoplasm
(hemangioma, inhibitors, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(hemangioma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Liver, neoplasm
(hepatoma, inhibitors, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Liver, neoplasm
(hepatoma, metastasis, inhibitors; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(hepatoma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Drug delivery systems
(immunoconjugates, radiolabeled; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Ovary, neoplasm
Testis, neoplasm
(inhibitors, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Ovary, neoplasm
Ovary, neoplasm
Testis, neoplasm
Testis, neoplasm
(inhibitors; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(kidney carcinoma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(leukemia; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(lung carcinoma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(lung carcinoma; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(lymphoma; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(mammary gland carcinoma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(mammary gland carcinoma; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(melanoma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(melanoma; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Mesothelium
Mesothelium
(mesothelioma, inhibitors, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(mesothelioma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Ovary, neoplasm
Testis, neoplasm
(metastasis, inhibitors; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antibodies
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal, radiolabeled; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(neck carcinoma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(neck, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Neck, anatomical
Neck, anatomical
(neoplasm, inhibitors, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Ear
Nose

L19 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2003 ACS (Continued)
(neoplasm, metastasis, inhibitors; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Bone, neoplasm
(osteosarcoma, inhibitors, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Bone, neoplasm
Bone, neoplasm
(osteosarcoma, inhibitors; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Bone, neoplasm
(osteosarcoma, metastasis, inhibitors; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(osteosarcoma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(osteosarcoma; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(ovary, metastasis; radioimmunoconjugate for use in human
tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
Antitumor agents
(ovary; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(pancreas carcinoma, metastasis; radioimmunoconjugate for
use in human tumor therapy and its prepn.)
INDEX TERM: Skin, disease
(pemphigus; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(prostate carcinoma, metastasis; radioimmunoconjugate for
use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(prostate carcinoma; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Anti-inflammatory agents
Antitumor agents
Hematopoietic precursor cell
Polymorphonuclear leukocyte
Radiotherapy
(radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Lymphocyte
(radiolabeled monoclonal antibody to; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: CD19 (antigen)
CD20 (antigen)
CD22 (antigen)

L19 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2003 ACS (Continued)
Carcinoembryonic antigen
ROLE: BSU (Biological study, unclassified); BIOL (Biological
study)
(radiolabeled monoclonal antibody to; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antibodies
Avidins
ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(radiolabeled; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(rectum carcinoma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Intestine, neoplasm
(rectum, carcinoma, inhibitors, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Kidney, neoplasm
(renal cell carcinoma, inhibitors, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(sarcoma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Hematopoietic precursor cell
(stem, radiolabeled monoclonal antibody to; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(stomach carcinoma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antigens
ROLE: BSU (Biological study, unclassified); BIOL (Biological
study)
(surface, of hematopoietic precursor cell; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(testis, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
Antitumor agents
(testis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Bone marrow
Bone marrow
(transplant; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Radionuclides, biological studies

L19 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2003 ACS (Continued)
ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(.alpha.- and .beta.-emitters; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: 135372-98-4, 1-97-Immunoglobulin (mouse MAKA .kappa.-chain anti-human tumor-associated antigen reduced) 135374-40-2, 1-119-Immunoglobulin (mouse MAKA heavy chain anti-human tumor-associated antigen reduced)
ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal antibody contg., radiolabeled; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: 58-85-5D, Biotin, conjugates with monoclonal antibodies 9013-20-1D, Streptavidin, radiolabeled 10098-91-6D, Yttrium-90, conjugate with monoclonal antibody, biological studies 13967-65-2D, Holmium-166, conjugate with monoclonal antibody, biological studies 14378-26-8D, Rhenium-188, conjugate with monoclonal antibody, biological studies 14913-49-6D, Bismuth-212, conjugate with monoclonal antibody, biological studies 14998-63-1D, Rhenium-186, conjugate with monoclonal antibody, biological studies 15755-39-2D, Astatine-211, conjugate with monoclonal antibody, biological studies 15757-86-5D, Copper-67, conjugate with monoclonal antibody, biological studies 15766-00-4D, Samarium-153, conjugate with monoclonal antibody, biological studies 121806-84-6D, reaction products with monoclonal antibodies and radionuclides
ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: 52-66-4D, complex with tin 60-24-2, 2-Mercaptoethanol 70-49-5D, Mercaptosuccinic acid, complex with tin 77-92-9D, Citric acid, complex with Sn(II), reaction with isothiocyanate derivs. 80-72-8 302-04-5D, Isothiocyanate, reaction with citric acid deriva. 622-78-6D, Benzyl isothiocyanate, reaction with citric acid 1429-50-1D, complex with Sn(II) 12385-13-6, Hydrogen radical, reactions 13472-33-8D, Sodium perrhenate, labeled with rhenium-188 14114-09-1 15827-60-8D, complex with Sn(II) 22541-90-8D, complex with alkyl compds., reactions 119733-46-9D, complex with Sn(II)
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: 135373-71-6, DNA (mouse MAKA 1-119-immunoglobulin heavy chain-specifying cDNA) 245325-70-6
ROLE: PRP (Properties)
(unclaimed nucleotide sequence; radioimmunoconjugate for

L19 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2003 ACS (Continued)
use in human therapy and its prepn.)

L19 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:635569 HCAPLUS
DOCUMENT NUMBER: 131:269049
TITLE: Human therapeutic applicable radioimmune conjugate and
method for its production
INVENTOR(S): Benes, Ivan Friedrich; Bosslet, Klaus; Maecke, Helmut R.
PATENT ASSIGNEE(S): Switz.
SOURCE: Ger. Offen., 12 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
INT. PATENT CLASSIF.:
MAIN: A61K051-10
SECONDARY: A61K039-395
INDEX: A61K103-00
CLASSIFICATION: 8-9 (Radiation Biochemistry)
Section cross-reference(s): 15
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19813687	A1	19990930	DE 1998-19813687	19980327
EP 972528	A2	20000119	EP 1999-106013	19990325 <--
EP 972528	A3	20021009		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6241961	B1	20010605	US 1999-280028	19990326
JP 11322634	A2	19991124	JP 1999-86723	19990329

PRIORITY APPLN. INFO.: DE 1998-19813687 A 19980327
DE 1999-19911329 A 19990315

ABSTRACT:
Radioimmunoconjugates of .alpha.-emitters (e.g. 211At, 212Bi) or .beta.-emitters (e.g. 90Y, 186Re, 188Re, 68Cu) with cytotoxic monoclonal antibodies are prepd. without the use of complexing agents by partial reductive cleavage with 2-mercaptoethanol and direct coupling of the radionuclide to the free SH groups on the antibody. The antibody may be of mouse, human, or other mammalian origin, and may be humanized, recombinant, fragmented, or intact. Treatment of malignancies, esp. of hematopoietic tumors, with these conjugates can replace high-dose chemotherapy and whole-body irradn. and is assocd. with less severe side effects. Thus, a monoclonal antibody (protein and cDNA sequences of heavy and light chain variable regions given) was cleaved with 2-mercaptoethanol, diafiltered under N2, freeze-dried, reconstituted with a reducing soln. contg. tetra-Na 1,1,3,3-propanetetraphosphonate Sn(II) complex, and labeled with Na188ReO4.

SUPPL. TERM: monoclonal antibody radiolabeling cancer treatment; radiotherapy tumor rhenium isotope antibody
INDEX TERM: Antibodies
ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)

L19 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2003 ACS (Continued)
INDEX TERM: 135372-98-4, 1-97-Immunoglobulin (mouse MAKA .kappa.-chain anti-human tumor-associated antigen reduced) 135374-40-2, 1-119-Immunoglobulin (mouse MAKA heavy chain anti-human tumor-associated antigen reduced)
ROLE: PRP (Properties)
(amino acid sequence of; therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: 135373-71-6, DNA (mouse MAKA 1-119-immunoglobulin heavy chain-specifying cDNA) 245325-70-6
ROLE: PRP (Properties)
(nucleotide sequence of; therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: 52-66-4D, tin(II) complexes 70-49-5D, tin(II) complexes 80-72-8 1429-50-1D, tin complexes 14114-09-1 15827-60-8D, tin complexes 22541-90-8D, Tin2+, complexes, reactions 59178-29-9 119733-46-9
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reducing agent; therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: 10098-91-6, Yttrium-90, biological studies 14158-27-1, Strontium-89, biological studies 14378-26-8, Rhenium-188, biological studies 14913-49-6, Bismuth-212, biological studies 14998-63-1, Rhenium-186, biological studies 15720-38-4, Copper-68, biological studies 15755-39-2, Astatine-211, biological studies 15766-00-4, Samarium-153, biological studies
ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: 60-24-2, 2-Mercaptoethanol
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: 245353-41-7, PN: DE19813687 SEQID: 24 unclaimed DNA
245353-43-9, PN: DE19813687 SEQID: 26 unclaimed DNA
245353-46-2, PN: DE19813687 SEQID: 28 unclaimed DNA
245353-49-5, PN: DE19813687 SEQID: 30 unclaimed DNA
245353-53-1, PN: DE19813687 SEQID: 32 unclaimed DNA
ROLE: PRP (Properties)
(unclaimed nucleotide sequence; human therapeutic applicable radioimmune conjugate and method for its prodn.)
INDEX TERM: 192433-87-7 192705-48-9
ROLE: PRP (Properties)
(unclaimed protein sequence; human therapeutic applicable radioimmune conjugate and method for its prodn.)
INDEX TERM: 144429-41-4 245107-31-7
ROLE: PRP (Properties)
(unclaimed sequence; human therapeutic applicable radioimmune conjugate and method for its prodn.)

L19 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2003 ACS (Continued)
(conjugates, with radionuclides; therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: Hematopoiesis
(disorders; therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: Immunoglobulins
ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(fragments, radiolabeled; therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: Drug delivery systems
(immunoconjugates; therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: Antitumor agents
(metastasis; therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: Antibodies
ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(monoclonal, radiolabeled; therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: Hematopoietic precursor cell
Polymorphonuclear leukocyte
(radiolabeled monoclonal antibodies to surface antigens on; therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: Antigens
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(surface, of hemopoietic system, radiolabeled monoclonal antibodies binding to; therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: Anti-inflammatory agents
Antitumor agents
Radiotherapy
(therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: Radionuclides, biological studies
ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(.alpha.- and .beta.-emitters; therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: 245107-24-8
ROLE: PRP (Properties)
(Unclaimed; human therapeutic applicable radioimmune conjugate and method for its prodn.)

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E11           2     EP972632/PN
E12           1     EP972633/PN

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E10           1     EE200000014/PN
E11           1     EE200000015/PN
E12           1     EE200000016/PN

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L20 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:50043 HCAPLUS
DOCUMENT NUMBER: 132:104773
TITLE: Radioimmunoconjugate for use in human therapy and its preparation
INVENTOR(S): Benes, Ivan Friedrich; Bosslet, Klaus
PATENT ASSIGNEE(S): Switz.
SOURCE: Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
INT. PATENT CLASSIF.:
MAIN: A61K051-10
CLASSIFICATION: 8-9 (Radiation Biochemistry)
Section cross-reference(s): 15, 63
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 972528	A2	20000119	EP 1999-106013	19990325 <--
EP 972528	A3	20021009		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
DE 19813687	A1	19990930	DE 1998-19813687	19980327
DE 19911329	A1	20000921	DE 1999-19911329	19990315

PRIORITY APPLN. INFO.: DE 1998-19813687 A 19980327
DE 1999-19911329 A 19990315

ABSTRACT:
A conjugate of a monoclonal antibody to cells of the hematopoietic system with an .alpha.- or .beta.-emitter is useful for treatment of malignant hematopoietic diseases. Suitable .alpha.-emitters are 211At and 212Bi, and suitable .beta.-emitters are 90Y, 188Re, 186Re, 67Cu, 166Ho, and 153Sm; the radionuclide is bound to the antibody with or without use of a complexing agent. The radionuclide is not an I isotope. The monoclonal antibody may bind
e.g. to a surface antigen of granulocytes or granulocyte precursors or to .gtoreq.1 epitope of CD66. Thus, a purified anti-CD66 monoclonal antibody was subjected to partial reductive cleavage with 2-mercaptoethanol and lyophilized.
This antibody was labeled with 188Re by mixing with a soln. of freshly prepd. Na188ReO4 in the presence of tetra-Na 1,1,3,3-propanetetraphosphonate Sn(II) complex. This conjugate, when administered i.v. to patients with chronic myeloid leukemia at 100 mCi/wk, accumulated in the bone marrow and led to a high rate of destruction of endogenous hematopoietic stem cells and 100% acceptance of autologous or allogeneic bone marrow transplants.

SUPPL. TERM: radioimmunoconjugate hematopoietic disease treatment; monoclonal antibody radionuclide conjugate leukemia; radiotherapy bone marrow disease
INDEX TERM: Lymphoma
(B-cell, radiolabeled monoclonal antibody to; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: CD antigens
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(CD66, radiolabeled monoclonal antibody to; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Histocompatibility antigens
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(HLA-DR, HLA-DR-10.beta., radiolabeled monoclonal antibody to; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(Kaposi's sarcoma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(bladder carcinoma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Transplant and Transplantation
Transplant and Transplantation
(bone marrow; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Bladder
Bladder
Kidney, neoplasm
Lung, neoplasm
Mammary gland
Neck, anatomical
Neck, anatomical
Pancreas, neoplasm
Pancreas, neoplasm
Prostate gland
Stomach, neoplasm
Stomach, neoplasm
(carcinoma, inhibitors, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Lung, neoplasm
Lung, neoplasm
Mammary gland
Mammary gland
Prostate gland
Prostate gland
(carcinoma, inhibitors; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Lung, neoplasm
Mammary gland
Prostate gland
(carcinoma, metastasis, inhibitors; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(colon carcinoma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(colon carcinoma; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Intestine, neoplasm
Intestine, neoplasm
(colon, carcinoma, inhibitors, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Intestine, neoplasm
(colon, carcinoma, inhibitors; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Intestine, neoplasm
(colon, carcinoma, metastasis, inhibitors; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Intestine, neoplasm
(colorectal, carcinoma, inhibitors, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Hematopoiesis
(disorders; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Hematopoietic precursor cell
(granulocyte-macrophage, monoclonal antibody to, radiolabeled; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Blood vessel, neoplasm
Blood vessel, neoplasm
(hemangioma, inhibitors, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(hemangioma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Liver, neoplasm
(hepatoma, inhibitors, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Liver, neoplasm
(hepatoma, metastasis, inhibitors; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(hepatoma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Drug delivery systems
(immunoconjugates, radiolabeled; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Ovary, neoplasm
Testis, neoplasm
(inhibitors, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Ovary, neoplasm
Ovary, neoplasm
Testis, neoplasm
Testis, neoplasm
(inhibitors; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(kidney carcinoma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(leukemia; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(lung carcinoma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(lung carcinoma; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(lymphoma; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(mammary gland carcinoma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(mammary gland carcinoma; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(melanoma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(melanoma; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Mesothelium
Mesothelium
(mesothelioma, inhibitors, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(mesothelioma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Ovary, neoplasm
Testis, neoplasm
(metastasis, inhibitors; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antibodies
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal, radiolabeled; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(neck carcinoma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(neck, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Neck, anatomical
Neck, anatomical
(neoplasm, inhibitors, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Ear
Nose

L20 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2003 ACS (Continued)
(neoplasm, metastasis, inhibitors; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Bone, neoplasm
(osteosarcoma, inhibitors, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Bone, neoplasm
Bone, neoplasm
(osteosarcoma, inhibitors; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Bone, neoplasm
(osteosarcoma, metastasis, inhibitors; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(osteosarcoma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(osteosarcoma; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(ovary, metastasis; radioimmunoconjugate for use in human
tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
Antitumor agents
(ovary; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(pancreas carcinoma, metastasis; radioimmunoconjugate for
use in human tumor therapy and its prepn.)
INDEX TERM: Skin, disease
(pemphigus; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(prostate carcinoma, metastasis; radioimmunoconjugate for
use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(prostate carcinoma; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Anti-inflammatory agents
Antitumor agents
Hematopoietic precursor cell
Polymorphonuclear leukocyte
Radiotherapy
(radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Lymphocyte
(radiolabeled monoclonal antibody to; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: CD19 (antigen)
CD20 (antigen)
CD22 (antigen)

L20 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2003 ACS (Continued)
Carcinoembryonic antigen
ROLE: BSU (Biological study, unclassified); BIOL
(Biological
study)
(radiolabeled monoclonal antibody to; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antibodies
Avidins
ROLE: BAC (Biological activity or effector, except
adverse);
BSU (Biological study, unclassified); THU (Therapeutic
use);
BIOL (Biological study); USES (Uses)
(radiolabeled; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(rectum carcinoma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Intestine, neoplasm
(rectum, carcinoma, inhibitors, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Kidney, neoplasm
(renal cell carcinoma, inhibitors, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(sarcoma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Hematopoietic precursor cell
(stem, radiolabeled monoclonal antibody to; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(stomach carcinoma, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antigens
ROLE: BSU (Biological study, unclassified); BIOL
(Biological
study)
(surface, of hematopoietic precursor cell; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
(testis, metastasis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Antitumor agents
Antitumor agents
(testis; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Bone marrow
Bone marrow
(transplant; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: Radionuclides, biological studies

L20 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2003 ACS (Continued)
ROLE: BAC (Biological activity or effector, except
adverse);
BSU (Biological study, unclassified); THU (Therapeutic
use);
BIOL (Biological study); USES (Uses)
(.alpha.- and .beta.-emitters; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: 135372-98-4, 1-97-Immunoglobulin (mouse MAKA .kappa.-chain anti-human tumor-associated antigen reduced) 135374-40-2, 1-119-Immunoglobulin (mouse MAKA heavy chain anti-human tumor-associated antigen reduced)
ROLE: BAC (Biological activity or effector, except
adverse);
BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal antibody contg., radiolabeled; radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: 58-85-5D, Biotin, conjugates with monoclonal antibodies 9013-20-1D, Streptavidin, radiolabeled 10098-91-6D, Yttrium-90, conjugate with monoclonal antibody, biological studies 13967-65-2D, Holmium-166, conjugate with monoclonal antibody, biological studies 14378-26-8D, Rhenium-188, conjugate with monoclonal antibody, biological studies 14913-49-6D, Bismuth-212, conjugate with monoclonal antibody, biological studies 14998-63-1D, Rhenium-186, conjugate with monoclonal antibody, biological studies 15755-39-2D, Astatine-211, conjugate with monoclonal antibody, biological studies 15757-86-5D, Copper-67, conjugate with monoclonal antibody, biological studies 15766-00-4D, Samarium-153, conjugate with monoclonal antibody, biological studies 121806-84-6D, reaction products with monoclonal antibodies and radionuclides
ROLE: BAC (Biological activity or effector, except
adverse);
BSU (Biological study, unclassified); THU (Therapeutic
use);
BIOL (Biological study); USES (Uses)
(radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: 52-66-4D, complex with tin 60-24-2, 2-Mercaptoethanol 70-49-5D, Mercaptosuccinic acid, complex with tin 77-92-9D, Citric acid, complex with Sn(II), reaction with isothiocyanate derivs. 80-72-8 302-04-5D, Isothiocyanate, reaction with citric acid derivs. 622-78-6D, Benzyl isothiocyanate, reaction with citric acid 1429-50-1D, complex with Sn(II) 12385-13-6, Hydrogen radical, reactions 13472-33-8D, Sodium perrhenate,
labeled
with rhenium-188 14114-09-1 15827-60-8D, complex with Sn(II) 22541-90-8D, complex with alkyl compds., reactions 119733-46-9D, complex with Sn(II)
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(radioimmunoconjugate for use in human tumor therapy and its prepn.)
INDEX TERM: 135373-71-6, DNA (mouse MAKA 1-119-immunoglobulin heavy chain-specifying cDNA) 245325-70-6
ROLE: PRP (Properties)
(unclaimed nucleotide sequence; radioimmunoconjugate for

L20 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2003 ACS (Continued)
use in human therapy and its prepn.)

L20 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:635569 HCAPLUS
DOCUMENT NUMBER: 131:269049
TITLE: Human therapeutic applicable radioimmune conjugate and
method for its production
INVENTOR(S): Benes, Ivan Friedrich; Bosslet, Klaus; Maecke, Helmut R.
PATENT ASSIGNEE(S): Switz.
SOURCE: Ger. Offen., 12 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
INT. PATENT CLASSIF.:
MAIN: A61K051-10
SECONDARY: A61K039-395
INDEX: A61K103-00
CLASSIFICATION: 8-9 (Radiation Biochemistry)
Section cross-reference(s): 15
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19813687	A1	19990930	DE 1998-19813687	19980327
EP 972528	A2	20000119	EP 1999-106013	19990325 <--
EP 972528	A3	20021009		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6241961	B1	20010605	US 1999-280028	19990326
JP 11322634	A2	19991124	JP 1999-86723	19990329

PRIORITY APPLN. INFO.: DE 1998-19813687 A 19980327
DE 1999-19911329 A 19990315

ABSTRACT:
Radioimmunoconjugates of .alpha.-emitters (e.g. 211At, 212Bi) or .beta.-emitters (e.g. 90Y, 186Re, 188Re, 68Cu) with cytotoxic monoclonal antibodies are prepd. without the use of complexing agents by partial reductive cleavage with 2-mercaptoethanol and direct coupling of the radionuclide to the free SH groups on the antibody. The antibody may be of mouse, human, or other mammalian origin, and may be humanized, recombinant, fragmented, or intact. Treatment of malignancies, esp. of hematopoietic tumors, with these conjugates can replace high-dose chemotherapy and whole-body irradn. and is assocd. with less severe side effects. Thus, a monoclonal antibody (protein and cDNA sequences of heavy and light chain variable regions given) was cleaved with 2-mercaptoethanol, diafiltered under N2, freeze-dried, reconstituted with a reducing soln. contg. tetra-Na 1,1,3,3-propanetetraphosphonate Sn(II) complex, and labeled with Na188ReO4.

SUPPL. TERM: monoclonal antibody radiolabeling cancer treatment; radiotherapy tumor rhenium isotope antibody
INDEX TERM: Antibodies
ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)

L20 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2003 ACS (Continued)
INDEX TERM: 135372-98-4, 1-97-Immunoglobulin (mouse MAKA .kappa.-chain anti-human tumor-associated antigen reduced) 135374-40-2, 1-119-Immunoglobulin (mouse MAKA heavy chain anti-human tumor-associated antigen reduced)
ROLE: PRP (Properties)
(amino acid sequence of; therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: 135373-71-6, DNA (mouse MAKA 1-119-immunoglobulin heavy chain-specifying cDNA) 245325-70-6
ROLE: PRP (Properties)
(nucleotide sequence of; therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: 52-66-4D, tin(II) complexes 70-49-5D, tin(II) complexes 80-72-8 1429-50-1D, tin complexes 14114-09-1 15827-60-8D, tin complexes 22541-90-8D, Tin2+, complexes, reactions 59178-29-9 119733-46-9
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reducing agent; therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: 10098-91-6, Yttrium-90, biological studies 14158-27-1, Strontium-89, biological studies 14378-26-8, Rhenium-188, biological studies 14913-49-6, Bismuth-212, biological studies 14998-63-1, Rhenium-186, biological studies 15720-38-4, Copper-68, biological studies 15755-39-2, Astatine-211, biological studies 15766-00-4, Samarium-153, biological studies
ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: 60-24-2, 2-Mercaptoethanol
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: 245353-41-7, PN: DE19813687 SEQID: 24 unclaimed DNA
245353-43-9, PN: DE19813687 SEQID: 26 unclaimed DNA
245353-46-2, PN: DE19813687 SEQID: 28 unclaimed DNA
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245353-53-1, PN: DE19813687 SEQID: 32 unclaimed DNA
ROLE: PRP (Properties)
(unclaimed nucleotide sequence; human therapeutic applicable radioimmune conjugate and method for its prodn.)
INDEX TERM: 192433-87-7 192705-48-9
ROLE: PRP (Properties)
(unclaimed protein sequence; human therapeutic applicable radioimmune conjugate and method for its prodn.)
INDEX TERM: 144429-41-4 245107-31-7
ROLE: PRP (Properties)
(unclaimed sequence; human therapeutic applicable radioimmune conjugate and method for its prodn.)

L20 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2003 ACS (Continued)
(conjugates, with radionuclides; therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: Hematopoiesis
(disorders; therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: Immunoglobulins
ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(fragments, radiolabeled; therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: Drug delivery systems
(immunoconjugates; therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: Antitumor agents
(metastasis; therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: Antibodies
ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(monoclonal, radiolabeled; therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: Hematopoietic precursor cell
Polymorphonuclear leukocyte
(radiolabeled monoclonal antibodies to surface antigens on; therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: Antigens
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(surface, of hemopoietic system, radiolabeled monoclonal antibodies binding to; therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: Anti-inflammatory agents
Antitumor agents
Radiotherapy
(therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: Radionuclides, biological studies
ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(.alpha.- and .beta.-emitters; therapeutic radioimmune conjugate and method for its prodn.)
INDEX TERM: 245107-24-8
ROLE: PRP (Properties)
(Unclaimed; human therapeutic applicable radioimmune conjugate and method for its prodn.)

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E5            1      WO8403700/PN
E6            1      WO8403701/PN
E7            1      WO8403702/PN
E8            1      WO8403703/PN
E9            1      WO8403704/PN
E10           1      WO8403705/PN
E11           1      WO8403706/PN
E12           1      WO8403707/PN

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L21           1 WO8403698/PN

=> d iall
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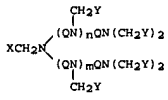
L21 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1985:166328 HCAPLUS
DOCUMENT NUMBER: 102:166328
TITLE: Chelating compound
INVENTOR(S): Mikola, Heikki; Mukkala, Veli Matti; Hemmila, Ilkka
PATENT ASSIGNEE(S): LKB-Produkter AB, Swed.; Wallac Oy
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.: C07C161-04; C07C101-26; C07F009-141; C07F009-65
CLASSIFICATION: 23-16 (Aliphatic Compounds)
Section cross-reference(s): 15, 78
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8403698	A1	19840927	WO 1984-SE89	19840313 <--
W: JP, US				
RW: AT, BE, CH, DE, FR, GB, LU, NL, SE				
SE 8301395	A	19840916	SE 1983-1395	19830315
EP 139675	A1	19850508	EP 1984-901128	19840313
EP 139675	B1	19870128		
R: DE, FR, GB, SE				
JP 60500767	T2	19850523	JP 1984-501184	19840313
JP 03077463	B4	19911210		
US 4808541	A	19890228	US 1987-16789	19870220

PRIORITY APPLN. INFO.: SE 1983-1395 19830315
WO 1984-SE89 19840313
US 1984-679047 19841108

GRAPHIC IMAGE:



I

ABSTRACT:
Chelating compd. I (Q = C2-8 alkylene; n, m = 0, 1; Y = carboxylic or phosphonic acid groups; X = active functional group permitting covalent coupling to a bioorg. mol.) was prepd. Thus, treating NH(CH2CH2NH2)2 with p-O2NC6H4CH2Br gave a mixt. of p-O2NC6H4CH2N(CH2CH2NH2)2 and H2N(CH2)2NH(CH2)2NHCH2C6H4NO2-p. Addn. of BrCH2CO2H to this mixt. gave p-O2NC6H4CH2N[CH2CH2N(CH2CO2H)2]2 and (HO2CCH2)2N(CH2)2N(CH2CO2H)CH2CH2N(CH2CO2H)CH2C6H4NO2-p. This mixt. was hydrogenated in the presence of Pd/C, then treated with C12CS to give the isothiocyanates. The chelating compd. N2-(p-isothiocyanatobenzyl)diethylenetriamine-N1,N1,N3,N3-tetraacetic acid was used to chelate Eu and to bind the Eu chelate to a monoclonal anti-AFP antibody. The Eu-antibody was used in the fluorescence immunoassay of AFP.

L21 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)

SUPPL. TERM: diethylenetriaminetetraacetic acid europium chelate; fluorescence immunoassay europium chelate
INDEX TERM: Immunochemical analysis
(fluorescence immunoassay, by use of (isothiocyanatobenzyl)diethylenetriaminetetraacetic acid europium complex)
INDEX TERM: 76177-16-7P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and catalytic hydrogenation of)
INDEX TERM: 95678-49-2P 95678-50-5P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and formation of europium chelates from)
INDEX TERM: 95678-49-2DP, europium complexes
ROLE: PREP (Preparation)
(prepn. and labeling of antibody by, in fluorescence immunoassay)
INDEX TERM: 95678-46-9P 95678-47-0P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction with bromoacetic acid)
INDEX TERM: 63563-84-8P 76177-16-7DP, europium complexes
95678-48-1DP, europium complexes
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction with thiophosgene)
INDEX TERM: 7440-53-1DP, N,N,N,N-tetraacetic acid, N-(4-nitrobenzyl)diethylenetriamine 95678-48-1P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
INDEX TERM: 463-71-8
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with (aminobenzyl)diethylenetriaminetetraacetic acid)
INDEX TERM: 100-11-8
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with diethylenetriamine)
INDEX TERM: 111-40-0
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with nitrobenzyl bromide)
INDEX TERM: 79-08-3
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with nitrobenzylated ethylenetriamine)

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L22           1 WO9006776/PN

=> d iall
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L22 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:95158 HCAPLUS
DOCUMENT NUMBER: 114:95158
TITLE: Preparation of macrocyclic aminophosphonic acid complexes of radionuclides as neoplasm inhibitors
INVENTOR(S): Simon, Jaime; Wilson, David A.; Garlich, Joseph R.; Troutner, David E.
PATENT ASSIGNEE(S): Dow Chemical Co., USA
SOURCE: Eur. Pat. Appl., 21 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K043-00
ADDITIONAL: C07F005-00
CLASSIFICATION: 1-6 (Pharmacology)
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
EP 375376	A2	19900627	EP 1989-313308	19891219	
EP 375376	A3	19910612			
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE					
US 5059412	A	19911022	US 1988-284876	19881219	
WO 9006776	A1	19900628	WO 1989-US5782	19891215	<--
W: AU, BR, DK, FI, HU, JP, KR, NO					
RW: AT, BE, CH, DE, ES, FR, GB, IT, LU, NL, SE					
AU 9048282	A1	19900710	AU 1990-48282	19891215	
AU 639899	B2	19930812			
EP 408701	A1	19910123	EP 1990-901464	19891215	
EP 408701	B1	19941012			
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE					
BR 8907255	A	19910312	BR 1989-7255	19891215	
HU 54897	A2	19910429	HU 1990-1163	19891215	
HU 207454	B	19930428			
JP 03502936	T2	19910704	JP 1990-501907	19891215	
ES 2061010	T3	19941201	ES 1990-901464	19891215	
JP 2515929	B2	19960710	JP 1989-501907	19891215	
CA 2005880	AA	19900619	CA 1989-2005880	19891218	
CA 2005880	C	19990105			
IL 92784	A1	19940826	IL 1989-92784	19891218	
AU 8947009	A1	19900621	AU 1989-47009	19891219	
CN 1046739	A	19901107	CN 1989-109819	19891219	
CN 1025983	B	19940928			
ZA 8909734	A	19910828	ZA 1989-9734	19891219	
DK 9001959	A	19900816	DK 1990-1959	19900816	
NO 9003632	A	19901017	NO 1990-3632	19900817	
NO 180434	B	19970113			
NO 180434	C	19970423			
AU 9350685	A1	19940224	AU 1993-50685	19931112	
AU 657641	B2	19950316			

PRIORITY APPLN. INFO.: US 1988-284876 A 19881219
US 1984-616985 B2 19840604
US 1985-738010 B2 19850528
US 1985-803376 B2 19851204
US 1987-50263 A2 19870514

L22 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)
WO 1989-US5782 A 19891215
OTHER SOURCE(S): MARPAT 114:95158
ABSTRACT:
153Sm, 159Gd, 166Ho, 177Lu, 90Y or 175Yb are complexes with macrocyclic aminophosphonic acids contg. the 1,4,7,10-tetraazacyclododecane moiety and having the N and P interconnected by (un)substituted alkylene. The complexes are useful in the treatment of bone-metastatic cancer. A refluxing mixt. of 3.48 g 1,4,7,10-tetraazacyclododecane, 17.2 mL conc. HCl, 7.2 g H3PO4 and 14 mL
water was treated with 13 g HCHO, to give 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetramethylphosphonic acid (DOTMP). This was complexed with 166Ho at pH 7-8, to give DOTMP-166Ho. Biodistribution studies of DOTMP-166Ho in rats showed strong accumulation in the bone.

SUPPL. TERM: radionuclide complex tetraazacyclododecane deriv anticancer;
bone cancer drug radionuclide complex
INDEX TERM: Radioelements, biological studies
ROLE: BIOL (Biological study)
(complexes with tetraazacyclododecanetetramethylphosphoni
c acid, for treatment of bone-marrow cancer)
INDEX TERM: Neoplasm inhibitors
(radionuclide complexes of tetraazacyclododecanetetrameth
ylphosphonic acid)
INDEX TERM: Bone, neoplasm
(metastasis, treatment of, with radionuclide complexes of
tetraazacyclodecanetetramethylphosphonic acid)
INDEX TERM: 10098-91-6DP, Yttrium-90, complex with tetraazacyclododecanetetramethylenephosphonic acid
13967-65-2DP, complex with tetraazacyclododecanetetramethyle
nephosphonic acid 14041-42-0DP, Gadolinium-159, complex with tetraazacyclododecanetetramethylenephosphonic acid
14041-44-2DP, Ytterbium-175, complex with tetraazacyclododecanetetramethylenephosphonic acid
14265-75-9DP, Lutetium-177, complex with tetraazacyclododecanetetramethylenephosphonic acid
29977-47-7DP, Samarium-158, complex with tetraazacyclododecanetetramethylenephosphonic acid
91987-74-5DP, complexes with radionuclides
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for treatment of bone cancer)
INDEX TERM: 39271-65-3, Yttrium chloride (90YCl3) 68052-85-7, Samarium
oxide (152Sm2O3) 132265-01-1, Holmium oxide (166Ho2O3)
132265-02-2, Gadolinium oxide (159Gd2O3)
ROLE: BIOL (Biological study)
(radionuclide complex of tetraazacyclododecane deriv. by,
for treatment of bone-marrow cancer)
INDEX TERM: 294-90-6, 1,4,7,10-Tetraazacyclododecane
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with formaldehyde and phosphoric acid in

L22 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)
antitumor agent prepn.)
INDEX TERM: 10294-56-1, Phosphorous acid, reactions
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with tetraazacyclododecane and formaldehyde
in antitumor prepn.)
INDEX TERM: 50-00-0, Formaldehyde, reactions
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with tetraazacyclododecane and phosphoric acid in antitumor prepn.)

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L23           1 WO9426753/PN

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L23 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:380314 HCAPLUS
DOCUMENT NUMBER: 122:160930
TITLE: Process for the preparation of azamacrocyclic or acyclic aminophosphonate ester derivatives
INVENTOR(S): Kiefer, Garry E.
PATENT ASSIGNEE(S): Dow Chemical Co., USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07F009-65
CLASSIFICATION: 29-7 (Organometallic and Organometalloidal Compounds)
Section cross-reference(s): 28
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9426753	A1	19941124	WO 1994-US5134	19940504 <--
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5714604	A	19980203	US 1993-65963	19930506
AU 9469086	A1	19941212	AU 1994-69086	19940504
AU 682190	B2	19970925		
EP 698029	A1	19960228	EP 1994-917333	19940504
EP 698029	B1	19981104		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE				
HU 73142	A2	19960628	HU 1995-3175	19940504
CN 1125949	A	19960703	CN 1994-192530	19940504
CN 1042537	B	19990317		
JP 08510249	T2	19961029	JP 1994-525620	19940504
AT 172978	E	19981115	AT 1994-917333	19940504
ES 2123137	T3	19990101	ES 1994-917333	19940504
RO 115883	B1	20000728	RO 1995-1927	19940504
PL 180756	B1	20010430	PL 1994-311651	19940504
CZ 290993	B6	20021113	CZ 1995-2890	19940504
RU 2135507	C1	19990827	RU 1995-122389	19940505
ZA 9403158	A	19951106	ZA 1994-3158	19940506
LT 3713	B	19960226	LT 1994-1925	19940506
LV 10867	B	19960820	LV 1994-99	19940506
FI 9505281	A	19951220	FI 1995-5281	19951103
NO 9504439	A	19960105	NO 1995-4439	19951106

PRIORITY APPLN. INFO.: US 1993-65963 A 19930506
WO 1994-US5134 W 19940504
OTHER SOURCE(S): CASREACT 122:160930; MARPAT 122:160930
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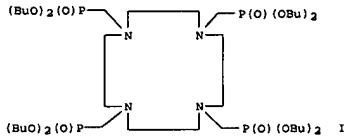
L23 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS (Continued)



I

ABSTRACT:
A novel process for the prepn. of azamacrocyclic or acyclic aminophosphonate ester derivs., e.g., I, is disclosed. The process concerns the reaction of an appropriate azamacrocyclic or acyclic primary or secondary amine with trialkyl phosphites and paraformaldehyde.

SUPPL. TERM: azamacrocyclic aminophosphonate; phosphonate azamacrocyclic acyclic
INDEX TERM: 50-00-0, Formaldehyde, reactions 102-85-2, Tributyl phosphite 107-15-3, Ethylenediamine, reactions
121-45-9,
Trimethyl phosphite 122-52-1, Triethyl phosphite
294-90-6, Cyclen 923-99-9, Tripropyl phosphite
78668-34-5 115078-43-8 161034-95-3
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of azamacrocyclic or acyclic aminophosphonates)
INDEX TERM: 154882-98-1P 160982-00-3P 160982-01-4P 160982-02-5P
161034-92-0P 161034-93-1P 161034-96-4P 161034-97-5P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of azamacrocyclic or acyclic aminophosphonates)
INDEX TERM: 1429-50-1P 137837-23-1P 160982-05-8P 160982-06-9P
160982-07-0P 161034-88-4P 161034-91-9P 161034-99-7P
161035-00-3P 161189-92-0P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of azamacrocyclic or acyclic aminophosphonates)

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E12           1      WO9511008/PN

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L24           2 WO9510940/PN

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L24 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:256814 HCAPLUS
DOCUMENT NUMBER: 124:299041
TITLE: Metal-based antimicrobial compositions.
INVENTOR(S): Jacobson, Howard W.; Scholla, Michael H.; Wigfall, Annie W.
PATENT ASSIGNEE(S): E. I. Du Pont De Nemours and Company, USA
SOURCE: U.S., 9 pp., Cont.-in-part of U.S. Ser. No. 6,002, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A01N025-26
US PATENT CLASSIF.: 424421000
CLASSIFICATION: 63-8 (Pharmaceuticals)
Section cross-reference(s): 5
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5503840	A	19960402	US 1993-139962	19931020
US 5180585	A	19930119	US 1991-742963	19910809
AU 9334412	A1	19940815	AU 1993-34412	19930111
EP 677989	A1	19951025	EP 1993-903055	19930111
EP 677989	B1	19980916		
R: DE				
JP 08505858	T2	19960625	JP 1993-516449	19930111
WO 9510940	A1	19950427	WO 1994-US6344	19940609 <--
W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2171703	AA	19950427	CA 1994-2171703	19940609
AU 9470544	A1	19950508	AU 1994-70544	19940609
AU 690563	B2	19980430		
EP 724388	A1	19960807	EP 1994-919377	19940609
R: BE, DE, ES, FR, GB, IT, NL				
JP 09504022	T2	19970422	JP 1994-511743	19940609

PRIORITY APPLN. INFO.:
US 1991-742963 19910809
US 1993-6022 19930115
WO 1993-US194 19930111
US 1993-139962 19931020
WO 1994-US6344 19940609

ABSTRACT:
An antimicrobial compn. is given, made of titanium dioxide, barium sulfate and/or zinc oxide particles, having successive coatings of silver, in some cases a coating of zinc and/or copper compds. such as zinc oxide, copper(II) oxide and zinc silicate, silicon dioxide, alumina, and a dispersion aid such as
dioctyl azelate. The compns. are esp. suitable for incorporation into plastics, and do not cause coloration or staining of the plastic.

SUPPL. TERM: metal antimicrobial compn plastic
INDEX TERM: Bactericides, Disinfectants, and Antiseptics

L24 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2003 ACS (Continued)
Fungicides and Fungistats
(metal-based antimicrobial compns.)
INDEX TERM: Plastics
ROLE: POF (Polymer in formulation); USES (Uses)
(metal-based antimicrobial compns. for)
INDEX TERM: 1314-13-2, Zinc oxide, biological studies 1317-38-0, Copper(II) oxide, biological studies 1344-28-1, Alumina, biological studies 7631-86-9, Silicon dioxide, biological studies 7727-43-7, Barium sulfate 13463-67-7, Titanium dioxide, biological studies 13814-85-2, Zinc silicate
ROLE: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metal-based antimicrobial compns.)
INDEX TERM: 126-30-7, Dimethylolpropane 2064-80-4, Dioctyl azelate.
ROLE: MOA (Modifier or additive use); USES (Uses)
(metal-based antimicrobial compns.)

L24 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:632329 HCAPLUS
DOCUMENT NUMBER: 123:27810
TITLE: Antimicrobial coated inorganic particles, for polymers.
INVENTOR(S): Jacobson, Howard Wayne; Scholla, Michael Heal; Wigfall, Annie Williams
PATENT ASSIGNEE(S): du Pont de Nemours, E. I., and Co., USA
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A01N059-16
SECONDARY: A01N025-26; A01N025-34; C08K009-10
CLASSIFICATION: 5-2 (Agrochemical Bioregulators)
Section cross-reference(s): 38
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9510940	A1	19950427	WO 1994-US6344	19940609 <--
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RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9334412	A1	19940815	AU 1993-34412	19930111
EP 677989	A1	19951025	EP 1993-903055	19930111
EP 677989	B1	19980916		
R: DE				
JP 08505858	T2	19960625	JP 1993-516449	19930111
US 5503840	A	19960402	US 1993-139962	19931020
AU 9470544	A1	19950508	AU 1994-70544	19940609
AU 690563	B2	19980430		
EP 724388	A1	19960807	EP 1994-919377	19940609
R: BE, DE, ES, FR, GB, IT, NL				
JP 09504022	T2	19970422	JP 1994-511743	19940609

PRIORITY APPLN. INFO.:
US 1993-139962 19931020
US 1991-742963 19910809
WO 1993-US194 19930111
US 1993-6022 19930115
WO 1994-US6344 19940609

ABSTRACT:
An antimicrobial compn. is given of Ti dioxide, Ba sulfate and/or Zn oxide particles, having successive coatings of Ag, in some cases a coating of Zn and/or Cu compds. such as Zn oxide, Cu(II) oxide and Zn silicate, as well as silica, alumina and a dispersion aid, such as dioctyl azelate. The compn. is dispersible in a polymer matrix, without adverse effects on polymer properties.

SUPPL. TERM: microbicide coated inorg particle polymer
INDEX TERM: Polymers, uses
ROLE: POF (Polymer in formulation); USES (Uses)
(antimicrobial compn. for)
INDEX TERM: Bactericides, Disinfectants, and Antiseptics
Fungicides and Fungistats
(antimicrobial compn. for polymers)
INDEX TERM: 1314-13-2, Zinc oxide, biological studies 1317-38-0, CopperII) oxide, biological studies 7440-50-8, Copper,

L24 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2003 ACS (Continued)
biological studies 7727-43-7, Barium sulfate 11126-29-7,
Zinc silicate 13463-67-7, Titanium dioxide, biological studies
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(antimicrobial compn. for polymers)
INDEX TERM: 77-99-6, Trimethylolpropane 1344-28-1, Alumina, uses 2064-80-4, Dioctyl azelate 7631-86-9, Silica, uses
ROLE: MOA (Modifier or additive use); USES (Uses)
(antimicrobial compn. for polymers)

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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Apr 08	"Ask CAS" for self-help around the clock
NEWS 3	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 4	Apr 09	ZDB will be removed from STN
NEWS 5	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 6	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 7	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 8	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 9	Jun 03	New e-mail delivery for search results now available
NEWS 10	Jun 10	MEDLINE Reload
NEWS 11	Jun 10	PCTFULL has been reloaded
NEWS 12	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS 13	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
NEWS 14	Jul 29	Enhanced polymer searching in REGISTRY
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NEWS 16	Aug 08	CANCERLIT reload
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NEWS 18	Aug 08	NTIS has been reloaded and enhanced
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NEWS 23	Sep 03	JAPIO has been reloaded and enhanced
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NEWS 26	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
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NEWS 48 Mar 04 SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 49 Mar 19 APOLLIT offering free connect time in April 2003
NEWS 50 Mar 20 EVENTLINE will be removed from STN
NEWS 51 Mar 24 PATDPAFULL now available on STN
NEWS 52 Mar 24 Additional information for trade-named substances without structures available in REGISTRY
NEWS 53 Mar 24 Indexing from 1957 to 1966 added to records in CA/CAPLUS

NEWS EXPRESS January 6 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS INTER General Internet Information
NEWS LOGIN Welcome Banner and News Items
NEWS PHONE Direct Dial and Telecommunication Network Access to STN
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:33:35 ON 01 APR 2003

=> fil reg
COST IN U.S. DOLLARS SINCE FILE ENTRY 0.21 TOTAL SESSION 0.21
FULL ESTIMATED COST

FILE 'REGISTRY' ENTERED AT 11:33:43 ON 01 APR 2003
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 31 MAR 2003 HIGHEST RN 501072-24-8
DICTIONARY FILE UPDATES: 31 MAR 2003 HIGHEST RN 501072-24-8

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

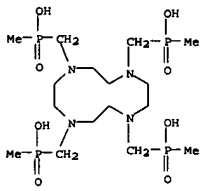
=> e dotmp/cn
E1 1 DOTMENT 324/CN

```
E2            1      DOTMENT 358/CN
E3            2 --> DOTMP/CN
E4            1      DOTORIOSIDE I/CN
E5            1      DOTORIOSIDE II/CN
E6            2      DOTP/CN
E7            1      DOTPME/CN
E8            1      DOTPP/CN
E9            1      DOTRIACOLIDE/CN
E10           1      DOTRIACONTA-15,17-DIYNE POLYMER/CN
E11           1      DOTRIACONTA-16,?-DIEN-15-ONE, 2,6,10,14,19,23,27,31-OCTAMETH
                     YL-/CN
E12           1      DOTRIACONTAAZADOTRIACONTABORA(4,6)FULLERANE-C64-C1/CN

=> s e3
L1            2 DOTMP/CN

=> d 1-
YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y
```

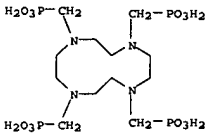
L1 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2003 ACS
RN 132446-35-6 REGISTRY
CN Phosphinic acid, [1,4,7,10-tetraazacyclododecane-1,4,7,10-tetrayltetrakis(methylene)]tetrakis[methyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1,4,7,10-Tetraazacyclododecane, phosphinic acid deriv.
OTHER NAMES:
CN **DOTMP**
FS 3D CONCORD
MF C16 H40 N4 O8 P4
CI COM
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMINFORMRX, CIN, PROMT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

13 REFERENCES IN FILE CA (1962 TO DATE)
6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
13 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L1 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2003 ACS
RN 91987-74-5 REGISTRY
CN Phosphonic acid, [1,4,7,10-tetraazacyclododecane-1,4,7,10-tetrayltetrakis(methylene)]tetrakis- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1,4,7,10-Tetraazacyclododecane, phosphonic acid deriv.
OTHER NAMES:
CN 1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetrakis(methylenephosphonic acid)
CN 1,4,7,10-Tetraazacyclododecane-N,N',N'',N'''-tetramethylenephosphonic acid
CN **DOTMP**
CN DOTP
CN N,N',N'',N'''-Tetrakis(phosphonomethyl)-1,4,7,10-tetraazacyclododecane
FS 3D CONCORD
MF C12 H32 N4 O12 P4
CI COM
LC STN Files: BEILSTEIN*, CA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, CIN, GMELIN*, MEDLINE, PROMT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

51 REFERENCES IN FILE CA (1962 TO DATE)
28 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
51 REFERENCES IN FILE CAPLUS (1962 TO DATE)

```
=> e holmium/cn
E1            1     HOLMIOSIDE/CN
E2            1     HOLMITE/CN
E3            1 --> HOLMIUM/CN
E4            1     HOLMIUM (HO3+)/CN
E5            1     HOLMIUM .ALPHA.-METHYLACRYLATE/CN
E6            1     HOLMIUM 0-0.3, TERBIUM 99.7-100 (ATOMIC)/CN
E7            1     HOLMIUM 0-23, TIN 77-100 (ATOMIC)/CN
E8            1     HOLMIUM 0-33.3, IRON 0-100, NICKEL 0-100 (ATOMIC)/CN
E9            1     HOLMIUM 0-40, MANGANESE 60-100 (ATOMIC)/CN
E10           1     HOLMIUM 0-50.0, IRON 50.0-100 (ATOMIC)/CN
E11           1     HOLMIUM 0-6.5, SILICON 93.5-100 (ATOMIC)/CN
E12           1     HOLMIUM 0-8, PALLADIUM 92-100 (ATOMIC)/CN

=> s e3
L2            1 HOLMIUM/CN

=> d
```

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN 7440-60-0 REGISTRY
CN **Holmium (8CI, 9CI)** (CA INDEX NAME)
OTHER NAMES:
CN Holmium-165
DR 24490-89-9, 110444-52-5
MF Ho
CI COM
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DETHERM*, DIOGENES, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, IFICDB, IFIPAT, IFIUDB, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PIRA, PROMT, TOXCENTER, ULIDAT, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

Ho

13880 REFERENCES IN FILE CA (1962 TO DATE)
1433 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
13892 REFERENCES IN FILE CAPLUS (1962 TO DATE)

```
=> fil .search
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                              14.68      14.89

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=> s l1 and l2
L3            4 L1 AND L2

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4            4 DUP REM L3 (0 DUPLICATES REMOVED)

=> d ibib ab hitstr 1-
YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):y
```

L4 ANSWER 1 OF 4 MEDLINE
ACCESSION NUMBER: 2002611223 MEDLINE
DOCUMENT NUMBER: 22255109 PubMed ID: 12368378
TITLE: High-dose 166Ho-DOTMP in myeloablative treatment of multiple myeloma: pharmacokinetics, biodistribution, and absorbed dose estimation.
AUTHOR: Rajendran Joseph G; Eary Janet F; Bensinger William; Durack
Larry D; Vernon Cheryl; Fritzberg Alan
CORPORATE SOURCE: Department of Radiology, University of Washington, Seattle,
Washington 98195, USA.. rajan@u.washington.edu
SOURCE: JOURNAL OF NUCLEAR MEDICINE, (2002 Oct) 43 (10) 1383-90.
Journal code: 0217410. ISSN: 0161-5505.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 20021008
Last Updated on STN: 20021031
Entered Medline: 20021030

AB Thirty-two patients with multiple myeloma were treated with high doses of 166Ho-1,4,7,10-tetraazacyclododecane-1,4,7,10-tetramethylene-phosphonic acid (DOTMP) and were a subset of patients enrolled in a multicenter phase
I/II dose escalation myeloablative trial. 166Ho with beta-emission (half-life, 26.8 h; beta-particle energies, 1.85 MeV [51%] and 1.77 MeV [48%]; gamma-photons, 80.6 keV [6.6%] and 1.38 MeV [0.9%]) was complexed to DOTMP, a macrocyclic tetraphosphonate. Pharmacokinetics, dosimetry, and
biodistribution were studied. METHODS: Patients were treated at escalating
dose levels of 20, 30, and 40 Gy to the bone marrow in combination with high-dose melphalan, with or without total-body irradiation, to evaluate toxicity and efficacy. After infusion with 1,110 MBq (30 mCi) of 166Ho-DOTMP for evaluation of biodistribution and dosimetry calculation, patients received the calculated amount of radioactivity for therapy in a single administration based on estimated dose calculations. RESULTS: Thirty-two patients participated in the study and were then treated. The average amount of administered radioactivity was 74.3 GBq (2,007 mCi) (range, 21.5-147.5 GBq [581-3,987 mCi]) of 166Ho-DOTMP. CONCLUSION: 166Ho-DOTMP has physical and pharmacokinetic characteristics compatible with high-dose myeloablative treatment of multiple myeloma.

L4 ANSWER 2 OF 4 MEDLINE
ACCESSION NUMBER: 93313213 MEDLINE
DOCUMENT NUMBER: 93313213 PubMed ID: 8324232
TITLE: Bone marrow transplantation in dogs after radio-ablation with a new Ho-166 amino phosphonic acid bone-seeking agent (DOTMP).
AUTHOR: Parks N J; Kawakami T G; Avila M J; White R; Cain G R; Raaka S D; Hornoff W; Fisher P; Moore P; Seibert J A; +
CORPORATE SOURCE: Institute for Toxicology and Environmental Health, University of California, Davis 95616.
SOURCE: BLOOD, (1993 Jul 1) 82 (1) 318-25.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199308
ENTRY DATE: Entered STN: 19930820
Last Updated on STN: 19950206
Entered Medline: 19930811

AB beta-emitting 166Ho (t1/2 = 26.78 hours, E(beta)max = 1.8 MeV) complexed with the phosphonic acid chelator, 1,4,7,10
tetraazacyclododecane-1,4,7,10-
tetra(methylene phosphonic acid) (DOTMP) at a ligand-to-metal ratio of 1.5:1 binds to bone. This radioactive complex is a marrow-ablating radiopharmaceutical that appears useful for preparation of bone marrow (BM) transplant recipients without the morbidity usually associated with total body irradiation preparatory regimens. We have found with seven splenectomized young adult beagle dogs that a 166Ho radiopharmaceutical dosage of 370 MBq/kg body weight provides an initial skeletal radioactivity burden of at least 1.5 GBq/kg skeleton and results in complete ablation of hematopoietic marrow cell populations within 7 days. The beta particle flux distribution in BM-forming skeletal tissue is not uniform. Red marrow radiation doses varied from 30 to 115 Gy as estimated by direct radioassay and autoradiographic analyses of both bone biopsies and postmortem samples; the median value of 61 Gy agreed with our theoretical expectations. In vivo radioactivity distribution was evaluated
with nuclear imaging methods. Apparently, normal hematopoiesis was restored in three dogs with autologous BM transplants performed 5 to 6 days after administration of the marrow ablative radiopharmaceutical, 166Ho-DOTMP. BM biopsies at 7 to 10 months posttransplantation indicate continued normal hematopoietic activity.

L4 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:222465 CAPLUS
DOCUMENT NUMBER: 116:222465
TITLE: The solution structure of Ln(DOTP)5- complexes. A comparison of lanthanide-induced paramagnetic shifts with the MMX energy-minimized structure
AUTHOR(S): Geraldes, Carlos F. G. C.; Sherry, A. Dean; Kiefer, Garry E.
CORPORATE SOURCE: Dep. Chem., Univ. Coimbra, Coimbra, 3049, Port.
SOURCE: Journal of Magnetic Resonance (1969-1992) (1992), 97(2), 290-304
CODEN: JOMRA4; ISSN: 0022-2364
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Complexes between the trivalent lanthanide ions and the macrocyclic chelate 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetra(methylene phosphonate) (DOTP) were examd. by high-resoln. NMR spectroscopy. The proton spectra of the diamagnetic La(DOTP)5- and Lu(DOTP)5- complexes provide evidence for very rigid chelate structures with the ethylenediamine-contg. chelate rings essentially locked into a single conformation at room temp. The activation energy for ethylenediamine chelate ring interconversions in these complexes is approx. 100 kJ/mol, considerably higher than that reported previously for the corresponding Ln(DOTA)- complexes (DOTA is the tetraacetate analog of DOTP). Lanthanide-induced shifts are reported for all 1H, 13C, and 31P nuclei in 11 Ln(DOTP)5- complexes. The proton spectra of these complexes display unusually large lanthanide-induced shifts, one showing a spectrum in which
the 1H resonances span 900 ppm. The contact and pseudocontact contributions to these shifts were sepd. using Reilley's temp.-independent
method and the resulting pseudocontact lanthanide-induced NMR shifts were in excellent agreement with those calcd. for a structure derived using MMX
mol. modeling methods. The pseudocontact shifts provide evidence for Ln(DOTP)5- chelates which have virtually identical structures along the lanthanide series, with the possible exception of Tm(DOTP)5-.

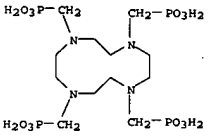
IT 7440-60-0D, Holmium, complexes with tetraazacyclodecanetetra(methy lenephosphonate) 91987-74-5D, lanthanide complexes
RL: PRP (Properties)
(soln. structure of, NMR in study of)

RN 7440-60-0 CAPLUS
CN Holmium (8CI, 9CI) (CA INDEX NAME)

Ho

RN 91987-74-5 CAPLUS
CN Phosphonic acid, [1,4,7,10-tetraazacyclododecane-1,4,7,10-tetrayltetrakis(methylene)]tetrakis- (9CI) (CA INDEX NAME)

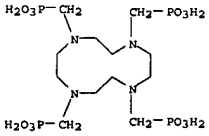
L4 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS (Continued)



L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1988:67563 CAPLUS
DOCUMENT NUMBER: 108:67563
TITLE: Phosphorus-31 and sodium-23 NMR lanthanide induced shifts in axially symmetric macrocyclic phosphonate complexes
AUTHOR(S): Sherry, A. Dean; Geraldes, C. F. G. C.; Cacheris, W. P.
CORPORATE SOURCE: Dep. Chem., Univ. Texas, Dallas, Richardson, TX, 75083-0688, USA
SOURCE: Inorganica Chimica Acta (1987), 139(1-2), 137-9
CODEN: ICHAA3; ISSN: 0020-1693
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 31P and 23Na lanthanide-induced NMR shifts (LIS) are reported for Ln(DOTP)5- complexes, where Ln is Ce, Pr, Nd, Sm, Eu, Tb, Dy, Ho, Er, Tm, or Yb, and DOTP is tetraazacyclododecane-N,N',N",N"'-tetramethylenephosphonate, along with some preliminary 1H and 13C NMR spectra which verify the rigidity of the complexes. The 23Na LIS values parallel theor. pseudocontact shift values for the Ln3+ cations. The pseudocontact contributions to both the 23Na and 31P shifts were estd. for all of the complexes. The origin of the structural change which occurs between Eu(DOTP)5- and Tb(DOTP)5- is discussed briefly.
IT **7440-60-0D**, complex with tetraazacyclododencanetetramethylenephosphonate **91987-74-5D**, lanthanide complexes
RL: PRP (Properties)
(NMR of phosphorus-31 and sodium-23 in, lanthanide-induced shift of)
RN 7440-60-0 CAPLUS
CN Holmium (8CI, 9CI) (CA INDEX NAME)

Ho

RN 91987-74-5 CAPLUS
CN Phosphonic acid, [1,4,7,10-tetraazacyclododecane-1,4,7,10-tetrayltetrakis(methylene)]tetrakis- (9CI) (CA INDEX NAME)



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* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:42:40 ON 01 APR 2003

=> fil reg
COST IN U.S. DOLLARS SINCE FILE ENTRY 0.21 TOTAL SESSION 0.21
FULL ESTIMATED COST

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 31 MAR 2003 HIGHEST RN 501072-24-8
DICTIONARY FILE UPDATES: 31 MAR 2003 HIGHEST RN 501072-24-8

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> e dotmp/cn
E1 1 DOTMENT 324/CN

```
E2            1      DOTMENT 358/CN
E3            2 --> DOTMP/CN
E4            1      DOTORIOSIDE I/CN
E5            1      DOTORIOSIDE II/CN
E6            2      DOTP/CN
E7            1      DOTPME/CN
E8            1      DOTPP/CN
E9            1      DOTRIACOLIDE/CN
E10           1      DOTRIACONTA-15,17-DIYNE POLYMER/CN
E11           1      DOTRIACONTA-16,?-DIEN-15-ONE, 2,6,10,14,19,23,27,31-OCTAMETH
                     YL-/CN
E12           1      DOTRIACONTAAZADOTRIACONTABORA(4,6)FULLERANE-C64-C1/CN

=> s e3
L1            2 DOTMP/CN

=> e holmium/cn
E1            1      HOLMIOSIDE/CN
E2            1      HOLMITE/CN
E3            1 --> HOLMIUM/CN
E4            1      HOLMIUM (HO3+)/CN
E5            1      HOLMIUM .ALPHA.-METHYLACRYLATE/CN
E6            1      HOLMIUM 0-0.3, TERBIUM 99.7-100 (ATOMIC)/CN
E7            1      HOLMIUM 0-23, TIN 77-100 (ATOMIC)/CN
E8            1      HOLMIUM 0-33.3, IRON 0-100, NICKEL 0-100 (ATOMIC)/CN
E9            1      HOLMIUM 0-40, MANGANESE 60-100 (ATOMIC)/CN
E10           1      HOLMIUM 0-50.0, IRON 50.0-100 (ATOMIC)/CN
E11           1      HOLMIUM 0-6.5, SILICON 93.5-100 (ATOMIC)/CN
E12           1      HOLMIUM 0-8, PALLADIUM 92-100 (ATOMIC)/CN

=> s e3
L2            1 HOLMIUM/CN

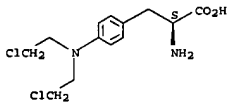
=> e melphalan/cn
E1            1      MELPERONE/CN
E2            1      MELPERONE HYDROCHLORIDE/CN
E3            1 --> MELPHALAN/CN
E4            1      MELPHALAN (RUSSIAN)/CN
E5            1      MELPHALAN ETHYL ESTER/CN
E6            1      MELPHALAN ETHYL ESTER HYDROCHLORIDE/CN
E7            1      MELPHALAN HYDROCHLORIDE/CN
E8            1      MELPHALAN ISOPROPYL ESTER/CN
E9            1      MELPHALAN METHYL ESTER/CN
E10           1      MELPHALAN-D-ALA-GLY-PHE-LEU-OH/CN
E11           1      MELPINTOL/CN
E12           1      MELPLATE ACTIVATOR/CN

=> s e3
L3            1 MELPHALAN/CN

=> d
```

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN 148-82-3 REGISTRY
CN L-Phenylalanine, 4-[bis(2-chloroethyl)amino]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Alanine, 3-[p-[bis(2-chloroethyl)amino]phenyl]-, L- (8CI)
OTHER NAMES:
CN 3025CB
CN Alanine nitrogen mustard
CN Alkeran
CN CB 3025
CN L-PAM
CN L-Phenylalanine mustard
CN L-Phenylalanine mustard hydrochloride
CN L-Sarcolysin
CN L-Sarcolysine
CN L-Sarkolysin
CN Levofalan
CN Levofolan
CN Levopholan
CN Melfalan
CN **Melphalan**
CN NSC 8806
CN Phenylalanine mustard
CN Sarcoclorin
FS STEREOSEARCH
DR 8057-25-8
MF C13 H18 Cl2 N2 O2
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR, PROMT, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2496 REFERENCES IN FILE CA (1962 TO DATE)
145 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2500 REFERENCES IN FILE CAPLUS (1962 TO DATE)
21 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS (Continued)

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=> fil .search
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    14.74      14.95

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=> d his

     (FILE 'HOME' ENTERED AT 13:42:40 ON 01 APR 2003)

     FILE 'REGISTRY' ENTERED AT 13:42:47 ON 01 APR 2003
                E DOTMP/CN
L1            2 S E3
                E HOLMIUM/CN
L2            1 S E3
                E MELPHALAN/CN
L3            1 S E3

     FILE 'MEDLINE, CAPLUS, BIOSIS, USPATFULL, EMBASE' ENTERED AT 13:43:24 ON
     01 APR 2003

=> s l1 and l2 and l3
L4            1 L1 AND L2 AND L3

=> d ibib ab
```

L4 ANSWER 1 OF 1 MEDLINE
ACCESSION NUMBER: 2002611223 MEDLINE
DOCUMENT NUMBER: 22255109 PubMed ID: 12368378
TITLE: High-dose 166Ho-DOTMP in myeloablative treatment of multiple myeloma: pharmacokinetics, biodistribution, and absorbed dose estimation.
AUTHOR: Rajendran Joseph G; Eary Janet F; Bensinger William; Durack Larry D; Vernon Cheryl; Fritzberg Alan
CORPORATE SOURCE: Department of Radiology, University of Washington, Seattle, Washington 98195, USA.. rajan@u.washington.edu
SOURCE: JOURNAL OF NUCLEAR MEDICINE, (2002 Oct) 43 (10) 1383-90. Journal code: 0217410. ISSN: 0161-5505.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 20021008
Last Updated on STN: 20021031
Entered Medline: 20021030

AB Thirty-two patients with multiple myeloma were treated with high doses of 166Ho-1,4,7,10-tetraazacyclododecane-1,4,7,10-tetramethylene-phosphonic acid (DOTMP) and were a subset of patients enrolled in a multicenter phase I/II dose escalation myeloablative trial. 166Ho with beta-emission (half-life, 26.8 h; beta-particle energies, 1.85 MeV [51%] and 1.77 MeV [48%]; gamma-photons, 80.6 keV [6.6%] and 1.38 MeV [0.9%]) was complexed to DOTMP, a macrocyclic tetraphosphonate. Pharmacokinetics, dosimetry, and biodistribution were studied. METHODS: Patients were treated at escalating dose levels of 20, 30, and 40 Gy to the bone marrow in combination with high-dose melphalan, with or without total-body irradiation, to evaluate toxicity and efficacy. After infusion with 1,110 MBq (30 mCi) of 166Ho-DOTMP for evaluation of biodistribution and dosimetry calculation, patients received the calculated amount of radioactivity for therapy in a single administration based on estimated dose calculations. RESULTS: Thirty-two patients participated in the study and were then treated. The average amount of administered radioactivity was 74.3 GBq (2,007 mCi) (range, 21.5-147.5 GBq [581-3,987 mCi]) of 166Ho-DOTMP. CONCLUSION: 166Ho-DOTMP has physical and pharmacokinetic characteristics compatible with high-dose myeloablative treatment of multiple myeloma.